Dissociation, Brain Function and Inflammation in Functional Neurological Disorder (FND)

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Abstract

Functional Neurological Disorder (FND) is a condition comprised of symptoms that alter motor and sensory functioning, leading to distress and impairments in bodily function which are distinct from other organic diseases. While theoretical models propose why the condition develops, the underlying mechanisms which distinguish how it develops are unclear. To date, there has been very little neurophysiological research into FND and even less research which considers FND from a biopsychosocial perspective. This thesis addresses a series of questions to help to understand the unique neurophysiology of FND and how it may be affected by psychological constructs (Dissociation), grouped into clusters of symptoms and the role of inflammation and altered neural connectivity: 1) Is dissociation a core construct in FND and how does this relate to other psychological correlates of chronic illness (stress, anxiety, depression, resilience, social isolation and social support) and outcomes (cognitive flexibility, hopefulness)? 2) Can the presence of potential subtypes of FND be statistically identified through Latent Class Analysis (LCA), and what are their relationships to dissociation types and predisposing factors? 3) What is the role of inflammation in FND, and how does this relate to dissociation? 4) Is inflammation in FND mediated by other facets of chronic illness including dietary inflammation, Body Mass Index (BMI) and mood? 5) Do baseline electroencephalographic (EEG) measures and Default Mode Networks (DMN) differ in FND? 6) What is the relationship between neural activity at baseline, inflammation and dissociation in FND? To answer these questions, a series of behavioural, EEG, and inflammatory responses were examined and modelled across three studies. Results suggest that dissociation is a discernible construct in FND as it is present across all studies; distinct clusters of symptoms can be statistically clustered to form subtypes, and these subtypes hold a relationship with types of dissociation in FND and predisposing factors as well as additional symptoms; inflammation is higher in those with FND, distinct pathways could indicate different models for the development of symptoms; Inflammation in FND can be both related to and independent of other facets of chronic illness but does hold a relationship with dissociation; baseline neural activity is distinctly different in FND and in particular in nodes associated with the DMN; there are relationships between baseline EEG measures, inflammation and dissociation in FND. Results are discussed in relation to chaos theory, allostatic load and conceptualisations of FND as an embodied brain disorder.

Declaration

This thesis comprises the candidate's own work and has not been submitted to this or any other University for a degree. The majority of the research, including data collection, analysis and write-up, was conducted by the candidate.

Statement of Contribution

This thesis represents the candidate's independent research. The candidate solely conducted the conceptualisation, design, data collection, analysis, and write-up of Study 1 (Chapter 5) and Study 2 (Chapter 6).

For study 3 (Chapter 7), which employed a multimodal design, the candidate was responsible for all aspects of EEG data collection, preprocessing, analysis, and interpretation, as well as the overall study design, statistical analysis, and write-up. Data collection was supported by a research associate, Bryony Heasman, whose role was limited to phlebotomy and blood sample collection. As phlebotomy falls outside the scope of traditional neuropsychology, this aspect of the study required specialised laboratory and biochemical expertise. This consideration was also given due to the ill health and neurological conditions of the candidate, which may, at times, have had serious ethical considerations in lone lab working and in blood sample collection. Nikki Stevenson provided further guidance on the chemical components of the analysis, offering technical oversight and support to the candidate and research associate as required.

Despite these contributions, the candidate conducted all aspects of the study design, data processing, statistical analysis, interpretation of findings, and thesis writing were conducted independently.

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Preface

"The fear of [this] disease used to terrify you when it was unknown to you" (Montaigne, 1595)

Someone who has FND does not receive the same benefits that a diagnostic label brings to others, such as an understanding of aetiology, symptom progression or access to healthcare, treatments and understanding from both professionals and family. I attempt to address this disparity throughout the review of the literature on FND. As a supporter of the community, whilst not entirely applicable to the majority of my studies, I felt this was something that needed addressing. Whilst a lot of the usual benefits that diagnostic labels bring may not be available to those with an FND diagnosis and knowledge that they have the condition alone may not cure them, there is at least the potential for reduced fear of what the illness means. Furthermore, a diagnosis can enable someone to feel part of a wider community, be part of a collective trying to identify what FND means and develop and share coping mechanisms. The same can be said of the general population and the medical sector, with reduced fear *should* come greater acceptance. I have dedicated my thesis and much of my career, to studying FND in the hopes of reducing stigma, promoting acceptance and awareness and addressing the gaps in knowledge that limit appropriate treatment and recovery for those with FND.

As is typical of scientific writing, at times, I limit descriptions throughout the thesis of FND to a description of symptoms, but FND should be viewed as more than this. FND is a reflection on the nature and relationship between health and illness, which is that, upon occasion, human beings need – for a brief time – to be ill. Throughout my third sector work, I have observed those with FND accept the management of symptoms for overall chronic reduction and develop the understanding that, at times, the body is 'sending a message'. This message could be that someone needs to slow down, rest, or allow the symptom to take control momentarily. FND is also a reflection on the unity of mind and body, psychophysical transparency and, finally, a biological reaction. Such considerations constitute the slow-changing taxonomy of FND and with such thought, we could lend ourselves to clearer descriptions and more widely accepted universal understandings of FND.

Before undertaking this PhD thesis, I thought I had a clear understanding of what FND was. I had, after all, been a patient myself after being diagnosed at 14 years old. I have also extensively studied and researched this condition at every opportunity during my academic

career thus far (and dedicated my undergraduate dissertation and master's thesis to this topic). Throughout my roles in the third sector (first as a support worker and later taking more strategic and management positions as the trustee of charities) I began to meet more and more patients. Suddenly, when the time was here and I had to write my early thesis chapters, I realised I no longer knew this condition at all. I felt I knew so little that it became a challenge to write the early chapters of my thesis. Whilst this omission is not something one would expect to find in a PhD thesis where I am supposed to be showing my expertise, it is, I feel, an essential omission to be transparent about.

Two issues contributed to this. The first was that the more patients I met, the more I realised that there was no one core defining symptom in FND and not only that, but no single symptom was a necessity. There was a rapid increase in those being diagnosed and FND became a more complex illness than it was already – one in which you could witness so many differences and worsening complexities of symptom presentation. I retreated to the literature, and herein, I found my second problem; even with growing interest and publications, opinion remained divided in the literature. Many sought to describe FND using the terms we have become familiar with, citing DSM removal of the need for psychological triggers, ICD frameworks or the classic "software vs hardware" analogies (a technique I have found myself falling into in the early chapters of my thesis, too). Yet no definition could succinctly and clearly define FND and its complicated substrates encompassing the true nature of this highly complex condition.

The more literature I critiqued and the more patients I met through my expanding roles, the less intelligible FND became to me. After one guest speech on the topic, I remember being utterly flustered when asked to provide a succinct definition of FND. I submerged myself in literature and re-emerged more knowledgeable in some ways and more confused in others. I decided to return to my patients, those whom I knew who had the best understanding of their illness narratives and really take note of their histories. Through this act, I found that the histories of those who live with FND held the answers. Every person with FND does not have one symptom, nor do they experience symptoms to the same degree of severity, and in each, there are subtle nuances and overlooked symptoms which are less obvious at first as others have taken over. In each patient, there are subtle disorders of presentation, speech and emotion, thought and every other convincible vegetative symptom. Every case history of FND can become an entire encyclopaedia of neurology, psychology and multiple other ologies if only we stop and spend the time attending to it.

As a psychologist, I cannot prematurely refute the role of emotion in FND as, by training, I have been encouraged to consider emotion as an underlying facet which weaves through our psychology, behaviour and biology and indeed, research consistently supports this too. However, I strongly feel that emotional experience has been explored archaically and in much too simplistic narratives to understand FND truly. For some people with FND, symptom experience is indeed drenched in emotional experience, and for some, emotional experience engulfs the entire history of the condition and could likely be a precipitating factor. However, this is certainly **not true of all patients with FND** nor true of all cases of relapse, onset or continuation of symptoms. An often-overlooked factor is that symptom onset is in itself an emotive experience – it is not always the source or the trigger, but it is often/always a result. As such, I will not discount the role of emotion throughout this thesis, but I will encourage all of those who research FND to be mindful of explorations in this area.

I consider FND throughout this thesis with a continual multi-perspective view. I feel it necessary to consider FND as a multifaceted structure whose forms are a product of the implicit repertoire of the nervous symptom as much as they are as an emotional or biological strategy, a disorder of neural network dysfunction or a disorder of the embodied brain. In Chapters 1 and 2, I consider exploring the current definitions of FND and potential subtypes as well as the potential underlying subtypes; in Chapter 3, I explore the how by exploring potential underpinning mechanisms and the experimental chapters that follow the aim to explore potential avenues of *why* FND occurs. I hope that these narratives and multi-perspective considerations are in the work that follows.

I invite you throughout to view FND as something which illuminates the entire range of biopsychosocial reactions by tirelessly reminding us of the continuity of mind and body mediated and underpinned by emotions and dissociation as a consequential defence (e.g. immunological) response. I also invite you to view this work as a stepping stone or singular puzzle piece in this complex and multifaceted area. This thesis does not hold all the answers (some readers may be disappointed to realise that it holds approximately six key findings given the word count). Nor is it a declaration that I hold all the answers (as I have already admitted at the beginning of this thesis that I am now only more aware of what I do not know). What springs to mind when I think of my knowledge of FND after writing this thesis can be summed by a quote from a lyrical legend, Alex Turner: "*What do you know, Oh' you don't know nothing, no*" (Arctic Monkeys, 2006). What I do hope is that this work can act as a catalyst for future research, and ignite conversation and investigations into FND.

Acknowledgements

My first debt is to those with FND, to whom I owe the possibility of this thesis. Thank you to everyone who has contributed to my studies, the time you have given to completing my experiments and for reminding me of the importance and necessity of this work. The FND community has embraced me and my research efforts in unimaginable ways, and I am forever grateful to them and to the UK charitable organisations (including FND Dimensions, FND Action and FND Friends) who strive to create and maintain these communities for supporting me in these research efforts. I'd particularly like to thank the patient advocates and support workers who strive to create space for those with FND, translate knowledge and, above all, provide a community and support for those diagnosed. Thank you for sharing and disseminating my research and study recruitment adverts and for welcoming me as a voice in this arena. I owe a great deal of my success to my work within FND Dimensions, who have banned me (temporarily) from all group chats and charity activity in an attempt to protect my time and ensure that I had the space I needed to complete my thesis. I hope that my working relationship with this charity will long continue.

To my Director of Studies, Professor Alex Sumich - I would like to thank you for the many years of tolerance, support and guidance. I proudly take the status of one of your more chaotic PhD students (if not the most). Not only have you offered me patience and supported me in enhancing my technical skills, but you have also provided me with guidance and opportunities throughout my career thus far. With your guidance, I have been able to craft a career that, at many times, looked impossible. Without you, this work would not have been possible. I owe you a world of thanks for your belief in me and for our continued working relationship and for the support you have given me in overcoming barriers and developing my skills as an academic.

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to name here but both staff and fellow PhD students (both past and present) have been essential throughout this journey. The connections formed in the SU and Horn in Hand over curly fries, pitches and data analysis have become so much more, a lifetime of love and friendship beyond this submission. My friends have been influential in supporting me throughout this journey, lending positivity and motivation and providing a space for me to vent or share ideas. I am grateful for the practical support: proofreading, childcare, lending me a space to recuperate or hide away and write, plying me with the best coffee and cooking me the most delicious roast potatoes. Every ounce of support you have all provided, near or from afar, has mattered (particularly the roast potatoes and occasional whisky and retreats). Some people arrive quietly and leave an imprint which comes to feel like home. Thank you for the warmth, kindness, humour, passion, the stillness, escape, the unexpected moments of peace and the moments that made even the hardest days feel a little lighter. Thank you, too, for holding space, for putting adventures on hold and future plans on pause, while the PhD demanded my focus and affection.

In addition, my colleagues and students at both NTU and BGU have been cheering me on throughout the final stages of my PhD. I'd like to thank you all for your continued motivation and support and for inspiring my continued practices as both a researcher and an academic. My special thanks to my previous boss, Dr Sue Becker, my previous tutor, Dr Maria Kontogianni and my internal assessor, Dr Nadja Heym, and to Prof Phil Banyard Mark Harris who continue to be great advocates and supporters of my work and who have all been willing to lend an ear when needed and provide space an opportunity for me to develop. My special thank you to Professor Eva Sundin who took it upon herself to become my informal mentor and who inspired me beyond words. What started as a working relationship turned into a powerful friendship and many beautiful moments which I shall cherish. Eva showed me the power of being a woman in science, in being (rather than avoiding) my authentic self in my practice and pedagogy and in advocating for those who needed a voice. It is through your bravery, commitment and fierce strength that I found my own narrative and that I found my authentic voice. Whilst Eva sadly passed away in the year of this thesis submission, everything she has taught me and inspired in me is embedded in the work. I know that she would be proud to see its eventual submission.

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This work could not have been completed without you. Your commitment and support deserve many bottles of prosecco, and as I have written it here, you can hold me to this debt.

Finally, to my son Lukas, this is for you. For someone so young, you are so full of wisdom. I do not need to ask if you are proud (you are telling me this repeatedly while I write this sentence). I am grateful for the time and space you have allowed me to complete this, your feedback and drawings on my drafts, and your continual cheering on, smiles on the rough days and for your unwavering love throughout. I hope that this work reminds you that **nothing** is beyond your reach and that your belief in me was one of the greatest gifts I carried throughout this journey.

Chapter 1: Conceptualisation of Functional Neurological Disorder & Models of Aetiology

1.1 Chapter Introduction

This chapter focuses on defining Functional Neurological Disorder (FND) and introduces key concepts of neurological and psychological significance in better understanding this illness. First, an overview of FND is given, including current definitions, symptom presentation, and theorised causes. Subsequent sections explore the historical perspectives of FND, which have contributed toward current understandings, conceptualisations and naming of the illness before moving onto contemporary models of aetiology and symptom generation. The chapter then explores current challenges and controversies within the field of FND, including the need to identify subtypes and predisposing factors and key considerations which should be considered in theoretical models, including dissociation as a prominent symptom.

1.2 Defining FND

FND is a condition in which symptoms of altered motor or sensory function cause distress and impairments to bodily function in conjunction with clinical findings incompatible with organic disease or other medical diagnoses (American Psychiatric Association, 2013). In FND, all areas of motor or sensory function can become impaired, and whilst diverse symptoms may be present, the most commonly reported are pain, fatigue, tremors, dystonia, gait abnormalities, motor or sensory disturbances, loss of feelings or functional seizures (Carson et al., 2016). Neurological assessment in those with FND shows a lack of organic disturbance and suggests that normal function is possible. Despite this feigning is not an adequate explanation for symptoms (Hallett et al., 2006). Presentation of symptoms is often further complicated by high rates of comorbidity with other neurological disorders, anxiety, depression, functional pain, fibromyalgia or other general somatic symptoms (Ani et al., 2013, Kozlowska et al., 2011, 2017). It has previously been considered to be an umbrella term owing to the vast array of neurological symptoms that the term encapsulates.

Whilst on the face of it, FND may seem like a catch-all term, these definitions of FND (which are littered throughout the literature) do not fully encapsulate the true nature and experience of the lived condition and are in part influenced by the historical treatment of FND in medical settings and research. The definitions of FND have also been constrained by limitations in neuroimaging technologies which have not allowed for in-depth assessment of neurological functioning and dated understandings of brain function. More recent understandings of FND acknowledge the plausibility of substantial alteration in brain function, with apparent gross changes in structure (Bègue et al., 2019; Voon et al., 2016). The Diagnostic and Statistical Manual of Mental Disorders (DSM-5, American Psychiatric Association, 2013) identifies the following criteria for FND:

- One or more symptoms of altered voluntary motor or sensory function;
- Where physical findings show evidence of incompatibility between the symptom and neurological or medical conditions;
- The symptom is not better explained by another medical or psychological disorder and;
- The symptom causes clinically significant distress or impairment in social, occupational or other areas of functioning

Of note, previous editions of the DSM required a psychological event as a trigger or predisposing factor for the onset of the disorder. This criterion has been dropped in DSM-V (American Psychiatric Association, 2013), with the recognition that a psychological trigger is not necessary for the development of FND symptoms. Many studies, for example, highlight that FND symptoms more commonly present with other types of predisposition or triggers including physical injury, and post-viral infection (Edwards et al., 2020; Reuber et al., 2002; Stone, Carson et al., 2009) and 37% of patients report physical injury within the months prior to onset of symptoms suggesting a need to reframe conceptualisations as trauma (Stone et al., 2010). Nevertheless, this change in the conceptualisation is subject to ongoing debate. Carson et al. (2011) highlight that many previous authors have argued that psychological distress is a primary precipitating factor prior to the onset of symptoms, and such focus has derailed the progression of more holistic understandings of FND beyond trauma enquiries. The International Statistical Classification of Diseases (ICD-11; WHO, 1992) sets out similar criteria for diagnosis of FND. A comparable difference between the two is the categorisation of the illness. Whilst the DSM-5 defines FND as a somatoform disorder, problematically

sandwiched between malingering and psychosomatic illnesses, the ICD categorises FND as a dissociative condition.

Refined conceptualisation and understanding of the psychological and biological mechanisms underpinning FND is becoming critical, particularly as it is currently one of the most common reasons for referral to neurology clinics and a leading cause of disability in working-age adults (Carson et al., 2011; Stone et al., 2010). FND is now more common than multiple sclerosis (MS; Carson et al., 2011). FND symptoms are, therefore, prevalent, extremely disabling and costly (Szaflarski et al., 2000, 2018). Yet FND continues to be viewed unfavourably in many medical circles, with neurologists rating FND as their least-liked condition, thought to stem from perceptions of lack of treatment options and the 'difficult' nature of the patient group (Carson et al., 2016; Evans & Evans, 2010) and implicit and explicit attitudes toward the legitimacy of FND prevalent in medical settings (Begley et al., 2023). This reflects the stigma experienced by those with FND and contributes to a sparse research base, despite the disabling symptoms and high prevalence (Carson et al., 2011). Often, patients are left unsure or questioning their diagnosis and fail to receive suitable and timely treatments, which influences treatment outcomes.

The ambiguity of FND classification is a major limitation in the development of theoretical models and research (Stephenson & Baguley, 2018). Diagnostic labels sometimes include references to symptomology subtypes. For example, in patients where seizures are present and lack epileptic origin, a diagnosis of FND with functional seizures may be given. In patients with movement difficulties, including gait, paralysis or coordination difficulties, a diagnosis of FND with Functional Movement Disorder (FMD) may be given. These symptom subtypes are inconsistent in diagnosis and are yet to be validated by empirical research. Even the naming of the condition has been ambiguous and caused significant controversy, producing stigma and limited research efforts. For example, functional seizures have, up until recently, been referred to as Non-Epileptic Attack Disorder or pseudo-seizures, both of which have negative connotations. FND has been referred to by many names, including conversion disorder, hysteria and medically unexplained symptoms. In the absence of a universally agreed-upon taxonomy, terminology tends to reflect subjective beliefs of illness causation (Kanaan et al., 2011; Sharpe & Carson, 2011), though it rarely relies on accurate data (Carson et al., 2016). Other synonyms for FND, including 'Medically Unexplained Symptoms' (which is the current NHS England's naming on their website and official documentation), "non-organic", and "pseudo seizures" state what the condition is not, rather than emphasising a likely indication

of cause (Stone et al., 2011). These “negative” diagnostic labels are based on an absence of research and poor understanding of FND and should be avoided, as they misrepresent FND as a completely unknown condition. However, several positive diagnostic indicators aid in the detection of FND, such as Hoover's sign for identifying functional weakness in voluntary control (McWhirter et al., 2011) and the typical semiology of functional seizures, which distinguish it markedly from other seizure conditions (Duncan, 2016). Nevertheless, further work that helps determine psychological and biological underpinnings will lead to clearer positive diagnostic criteria.

In any case, FND is currently the most accepted term by the patient, academic and clinical community (Carson et al., 2011), as it minimises stereotypical assumptions of aetiology, instead implicating a functional disruption. It is, therefore, the term that will be used throughout the current thesis. The prefix “functional” is used to indicate an issue with the workings of, rather than the structure of, the nervous system. Whilst originally researchers proposed the name change with the intention to make no assumption of aetiology (Feinstein, 2011; Edwards et al., 2020), recent meta-analyses of functional neuroimaging studies in FND have implicated altered activity in a number of brain regions associated with motor planning, selection and autonomic responding which are suggestive of issues with functioning (Boeckle et al., 2016). Patients with Functional Seizures also prefer the pre-fix of ‘Functional’ over ‘Non-Epileptic Attack Disorder’ finding it less offensive than psychological or negative labels (Stone et al., 2003). However, the term Functional is not without issue, there is now evidence of structural brain differences in patients with Functional Seizures (McSweeney et al., 2017), grey matter abnormalities in children and adolescents with FND (Kozlowska et al., 2017) and reduced white matter in comparison to healthy controls (Diez et al., 2019). Current neuroimaging techniques remain somewhat dated and limited and are yet to elucidate the true nature of the structural alterations present in FND, and whilst such alterations are likely, careful thought needs to be given to the limitations of the “software” vs “hardware analogy. The biopsychosocial sphere in which FND symptoms transcend is adaptive, as is the functioning of the nervous system as a biological system in which some patterns of functioning can cause structural changes, and this has been recently seen in FND (Begue et al., 2019; Coebergh et al., 2024). Nevertheless, the current limitations of a more appropriate term mean that FND will be used throughout this thesis as the least problematic.

Perplexing models and labels of such medically unexplained symptomology may reflect a dearth of understanding of a complex psychophysiological disorder (Raynor & Baslet,

2021). Whilst FND is commonly explained as resulting from the impact of psychological stressors on unconsciously produced symptomology (Brown et al., 2006; Roelofs et al., 2005), many patients do not report psychological stressors prior to, or at the time of, onset of symptoms (Ashkorb et al., 2013; Morsy et al., 2021; Pareés et al., 2014). Moreover, there are relatively few differences in self-reported adverse life events or abuse (sexual or physical) in patients with FND relative to healthy controls or patients with organic disorders (Kranick et al., 2011). A continual focus on finding a trauma in those who do not report psychological trauma is potentially damaging and traumatic in itself for those diagnosed both in clinical practice and in research. Of course, such arguments can be counteracted circularly Brown (2006) made the assumption that no trauma can be found because this traumatic experience has been suppressed in contemporary alterations of psychodynamic theories of FND. However, this argument does not allow for all of those who experience traumatic experiences and do not go on to develop FND. Nor is this the simplest or most scientific explanation; if emerging data does not support that a psychological trauma should be present at the onset of symptoms then attention should be drawn more widely to the mechanisms that could be unpinning FND (Hudson, 2020; Edwards et al., 2020). This is not to say that those mechanisms are unaffected by psychological trauma, but that they may be influenced by many other factors, and that a fixation and insistence on continual claims of FND as a purely psychological condition limits all avenues to investigation. Furthermore, this "psychological fixation" overshadows biological and social factors which are likely involved in the genesis and maintenance of FND symptoms (Ejareh dar & Kanaan, 2016). Thus, recent additions of the main classification systems for diseases (DSM-5 and ICD-10) have removed the diagnostic requirement of the presence of a psychological stressor (Pareés et al., 2014).

Classifications now conceptualise FND as a functional disorder, one that is not always caused by trauma. In line with such a framework, functional metaphors are often used when discussing FND with patients and family members – such as framing symptoms as a "software" rather than a "hardware" problem, reflecting ideologies of a structurally sound neural system with abnormal functionality. Individual analysis of Computed Tomography (CT) and Magnetic Resonance Imagining (MRI) data supports such claims; rarely are structural abnormalities present in FND nor they do not account for patterns of impairment (Kozlowska et al., 2015). Whilst psychological factors may not be necessary for causation, it is recognised that FND leads to a greater comorbidity of psychological conditions after the onset of symptoms (Carson

et al., 2011; Stone et al., 2010). These phenomena and the role of psychological correlates in FND is explored in greater depth in chapter 2 of the current thesis.

1.3 Epidemiology

FND is a common cause of disability particularly in neurological practice; FND is now the second most common reason for referral to neurology after migraines (Stone et al., 2010). If we want to be even more specific, FND accounts for 5 – 10% of new neurological consultations with an estimate of incidence rate at 12 per 100,000 per year (Carson et al., 2011). Based on this, Bennett et al., (2021) estimate that 50,000 – 100,000 people in the community have FND and that around 8,000 new diagnoses are made of FND per year in the UK. If other functional disorders (including irritable bowel syndrome and chronic pain syndromes) were also represented in such figures, cases would be even higher and these figures also don't account for the slow rate of diagnosis (which currently stands somewhere around 5 - 8 years; Kerr et al., 2016) or the slow progression from primary to secondary care which show that symptoms are present for many years and illness outcomes are hard to predict (Gelauff & Stone, 2016). Nor do these figures and estimated costs consider transient symptoms in primary care or emergency settings. FND is prevalent, and costly and results in high levels of disability and distress for those diagnosed and yet remains relatively unheard of.

There are variable reports for typical age of onset within the literature, some claim that FND commonly first presents in adolescence or early adulthood (Ani et al., 2013; Kozlowska et al., 2007) and others cite typical age of onset at 37 – 50 years (Factor et al., 1995; Morgante et al., 2012) or pubertal years (Canavese et al., 2012). However, of worthy note is that more recent literature demonstrates that FND can occur across all ages (though it is less common before 10 years old; Ferrare & Jankovic, 2008,). Different phenotypes do tend to deviate with the age of onset; paediatric patients often have walking abnormalities, functional seizures or visual disturbances (Ferrara & Jankovic, 2008), whilst other motor and sensory symptoms become more frequent in those over 20 years (Ellenstein et al., 2011). The time course of FND is variable ranging from transient symptoms to permanent dysfunction. Recovery occurs in 50 – 60% of patients, though spontaneous recovery is more common in children (percentage unknown; Stone et al., 2003; Gelauff et al., 2014; Kozlowska et al., 2017).

One area of epidemiology that is rarely disputed is the disproportional impact on women. Women are more commonly diagnosed with FND than men at a rate of 3:1 (Bennett, 2021), and women are disproportionately affected by FND across phenotypes with rates of around 70% in most studies (Gelauff et al., 2014). The history of FND is a further commentary on themes of maltreatment of women in medical practice and particularly in FND (Walusinski, 2014). Previous and dated terminology, including hysteria, for example, were used to denote this as not only a female affliction but also as a commentary on the view of females within medical practice. Many claim the diagnosis was more frequently applied to women as a means of brushing aside this female complaint (Maines & Maines, 2001; Verhaeghe, 2013), which also degrades the many males who are also diagnosed. Further, there is a lack of literature on cases and treatment of FND during pregnancy – a gap in research which needs urgently to be addressed given the practical risks during pregnancy and childbirth to both women and children.

Historical biases may make physicians more likely to diagnose FND in women than in men, despite similar symptom profiles (Edwards & Aybek, 2020; Marin et al., 2017). This bias is also exemplified in the different terminology used to describe hysteria in women and men, with those in males now being more widely and credibly recognised, such as post-traumatic stress disorder and health anxieties, which categorically distance themselves from what is now FND and the prejudice associated with it too. Further, there is a lack of recognition within the literature of non-binary or trans identities or other marginalised groups, including race and ethnicity, which present gaps in need of further and urgent exploration. If we are to study demographics and if such demographics are studied in other illness narratives, these too should be transparent and articulated within FND literature.

Despite the gender disparity and shared clinical symptoms etiological risk factors may vary and some small differences have been noted. Symptom onset and diagnosis is thought to occur at an older age in men (Duncan, 2016). Men with FND have been shown to display greater healthcare anxieties whilst women with FND have higher rates of environmental stress and family dysfunction (Reuber et al. et al., 2007). Though such differences are more likely a comment on sociological rather than aetiological factors and as such are not contributors to models of development of FND.

Studies do however claim that a larger proportion of those with FND come from lower socioeconomic backgrounds (Deka et al., 2007; Folks et al., 1984; Kuloglu et al., 2003) as is

often attributed to disparity in women's healthcare globally. However, there is a huge lack of recognition and massive misinterpretation of the data here that around 50% of those who develop FND need to reduce or give up employment (Carson et al., 2011) and that this is the result of, rather than a contributing factor, for development of FND further highlighting the impacts of the illness as opposed to the cause. Further, such arguments are stigmatising and blame those with FND for their own condition (i.e. if they were not born to socio-economically deprived families they would not have become ill). Environmental factors rather than wealth and a lack of education could contribute toward this increase including poor diet, pollutants and toxins, chronic stress and increased inflammation.

Economic disadvantage and a disproportionate effect on females could be attributed not socially but biologically to the development of FND. Current estimates do suggest a female-to-male sex ratio of 2 – 3:1 (Carson, 2016). However, a recent study exploring functional seizures indicated that the proportion afflicted increased with age at onset (Goldstein et al., 2019). There could however be a multitude of explanations for this including physician bias against diagnosing FND in men (Morgante et al., 2012), that women are more likely to present in healthcare services earlier than men (Carson, 2016) and that elevated levels in women might reflect complex differences in exposures to social and environmental risk factors including high rates of sexual abuse, intimate partner violence and sexual assault (Borumandnia et al., 2020; Stoltenborgh et al. et al., 2011). Ludwig et al., (2018) found that life events were experienced by patients with FND eight times as frequently as healthy controls. However, there may be more hidden gender-weighted risk factors outside of trauma that are important in understanding the aetiology of FND, including societal and familial expectations, which could have been partly encapsulated in previous studies (e.g. Morsy et al., 2022). Whilst understudied in FND, being in a caregiving role is associated with higher rates of mental and physical health impairment and higher rates of infection, including viral infection, whereby women are disproportionately affected (Pinquart & Sörensen, 2006; Schulz & Sherwood, 2008). Women are more likely than males to develop infections and there are more likely hormonal influences for women (Dias et al., 2022; Ingersoll, 2017; Van Lunzen & Altfeld, 2014). which are of important note in the considerations of this thesis. However, limited research funding into this area of epidemiology has instead led to speculation of social rather than important biological factors.

1.4 Models

Functional Neurological Disorder (FND) has been discussed in ancient Greek and Egyptian literature for millennia, often referred to as the "roaming uteri theory" and believed to primarily affect women. Throughout history, renowned scholars and thinkers such as Plato, Charcot, and Freud have added to the discourse surrounding FND, each offering their unique insights and terminology. From outlandish explanations to closed-minded views which do not encapsulate the full spectrum of FND symptoms and possible triggers, historical understandings of FND have been inadequate in fully comprehending its complexities. Although the causes and underlying mechanisms of FND still remain poorly understood, various models have been proposed (Vuilleumier, 2014). In the aforementioned realm of controversy that remains, and with a continued absence of universally agreed taxonomies, many of these theories tend to reflect passionately held beliefs about FND with minimal scientific supporting evidence (Kanaan et al., 2011). Recent theories of FND adopt a multi-factorial perspective in which psychological, biological, social and environmental components have the potential to influence and predispose individuals to FND, precipitate symptoms or have a role in maintaining or perpetuating the symptoms (Reuber et al., 2007). Such theories differ on the extent to which they believe each factor influences these areas or the lens from which they explore FND (in an attempt to explain either the aetiology or maintenance of symptoms). Theories of FND are still in their infancy and there remains little evidence of the emergence of a comprehensive or dominant model.

1.4.1 Historical accounts

While this thesis aims to be concise and will not cover all historical aspects, the work of Jean-Martin Charcot (1892) is of significant interest. Charcot's focus on Functional Symptoms inspired diagnostic strategies that are still utilised today. According to Charcot, dissociation - a separation of conscious and unconscious processes - could lead to dysfunctions of motor and sensorimotor systems. In the early 20th century, renowned physicians like Freud and Breuer expanded on Charcot's ideas, suggesting that the FND could be caused by psychological factors. They coined the term "conversion disorder" and used hypnosis as a diagnostic tool, proposing that physical symptoms resulted from repressed emotional issues that transformed into bodily complaints. These theories placed greater emphasis on the

psychological aspect than Charcot's. More recent iterations of such theories have incorporated evolutionary psychology and suggest that FND stems from primitive behaviours like motor arrest, freezing, and playing dead, originating from circuits within the basal ganglia and periaqueductal grey under the control of cortical and subcortical limbic regions (Nijenhuis et al., 2004; Whitlock, 1967). Evolutionary theories propose that FND is a response to a trigger leading to an exhibition of the body's primitive response mechanisms to stress. However, these theories rely mostly on empirical evidence and are challenging to test. Moreover, many patients do not report psychological triggers at the onset meaning that such theories could only apply to a small proportion of those diagnosed.

Historical accounts of conversion disorder have been revived with neurobiological evidence and animal studies related to defence mechanisms (see Cretton et al., 2020., for review). However, even contemporary models fail to consider a fully holistic view of the neurological and psychological antecedents in FND, and even contemporary conversion models fail to account for the low rates of previous traumatic experiences reported by many (in some as low as 15%; Aybek et al., 2017; Roelofs & Spinhoven, 2005; Sharpe & Faye, 2006) the absence of clear psychological triggers challenges the validity of this theory. Further research has shown that there are neurobiological abnormalities in individuals with FND, including evidence of alterations in brain structure and function (as reviewed in further detail in Chapter 3; Begue et al., 2019; Diez et al., 2021) even in those without reported traumatic experiences, suggesting an underlying dysregulation rather than a simple conversion of psychological distress. High comorbidity with other established neurological disorders, including epilepsy and movement disorders (Butler et al., 2021; Carle-Toulemonde et al., 2023; Ducroizet et al., 2023), suggests that FND likely has a neurobiological basis, rather than being solely a manifestation of psychological distress.

Thus, more recent research aims to comprehend the underlying cognitive processes of FND symptoms. As the cognitive system is organised hierarchically, with most perceptual and behavioural processing occurring automatically (Ashby et al., 2007; Atienza et al., 2002; Bargh & Chartrand, 1999; Legrain et al., 2009; Schneider & Chein, 2003), it is suggested that symptoms may result from lower-level pre-conscious processing systems (Edwards et al., 2012; Voon et al., 2016). Consistent with such theories, Bakvis et al., (2009) found evidence of altered, preconscious threat processing in patients with Non-Epileptic Attack Disorder (NEADs, a distinct seizure disorder under the FND umbrella). In this study, participants who had been sexually abused were more likely than non-abused patients to have their attention

drawn to angry faces presented beyond conscious thought. However, not all patients with NEADs or FND have experienced sexual trauma, and not all victims of sexual trauma go on to develop FND. Furthermore, it is likely that survivors of sexual assault would show such a response making associations with FND limited.

1.4.2 Integrative Cognitive Model of Medically Unexplained Symptoms

In 2006, Brown proposed the Integrative Cognitive Model of Medically Unexplained Symptoms (MUS), which posits FND as a disorder of perception and control involving mechanisms such as conversion, and somatisation. According to this theory, patients acquire "rogue representations" of their symptoms through various means, including their own physical illness history, exposure to illness in others, sociocultural transmission, or verbal suggestion. A malfunctioning attentional control system persistently activates and selects these "rogue representations," resulting in symptoms that are marked by altered perception (e.g. pain, anaesthesia, visual disturbance) or impaired control (e.g. tremor). The patient may misinterpret these symptoms as physical illness, creating a sense of loss of agency and involuntary symptoms.

Computational neuroscience has provided an explanation of the mechanism of FND based on predictive coding theories (Edwards et al., 2012; Van den Bergh et al., 2017). In this framework, the brain generates probabilistic internal models to infer the causes of sensory inputs (called posterior beliefs), which are based on prior expectations (learned knowledge) about the world and current sensory input. If there is a mismatch between prior expectations and sensory data, the brain tries to reduce the "prediction error" either by adjusting the prior expectation to fit the sensory data better or by adjusting the representation of sensory data to fit the prior expectation better (for example, by increasing or decreasing attention). This process is iterative and continuous, moving through a hierarchical structure, with lower levels representing basic features of sensory input and higher levels representing more complex properties.

Bottom-up prediction errors depend on top-down input from predictions (which can also be influenced by previous prediction errors). As time goes on, predictions and prediction errors build a level of confidence (variance around a mean distribution), which can be thought of as "precision" (smaller variance means greater precision). Precise prior expectations represent strong predictions, and the stronger the prior expectation, the more likely it is that the inferred cause of the sensory input (posterior) will be weighted in favour of the prior prediction.

Conversely, if the sensory input is highly precise, the posterior will be biased toward the sensory data. As more sensory inputs are accumulated over time, the prior will be updated to reflect the sensory data. Additionally, the system weights prediction errors based on how likely they are to be a result of noise or an accurate reflection of input. When precise sensory data is expected (e.g., in the light), the posterior will be weighted more in favour of sensory input. However, if the sensory input is expected to be imprecise or noisy (e.g., in the dark), the posterior will remain biased toward the prior. Ultimately, this process generates an optimal posterior model to infer the cause of sensory inputs.

These models tend to oversimplify the complex interplay between the psychological, biological, environmental and social factors. In Brown's model for example, there are no notable references to neurobiological concepts, and it is unclear what is wholly meant by these 'rogue mental representations'. Further, emotional and other internal states are known to influence symptomology. In addition, and in an adaptation to this theory, Brown & Reuber (2016) apply a similar theoretical framework to Functional Seizures and consider a "seizure scaffold" as a central symptom in which automatic activation of seizure behaviour occurs from memory and during arousal as a result of threat processing. Primary failure of interface in FND may not be due to abnormal prior expectations, but rather a failure to integrate information from multiple sensory modalities.

1.4.3 The Bayesian Model

Edwards et al. (2012) proposed a neurobiological model for FND termed the Bayesian account. This model proposes that Functional symptoms are the result of actions based on inferences. These interferences are mediated by expectations of symptom generation, past emotional and illness experiences and particularly body-focused attention, some of which have been outlined earlier. Functional symptoms are known to be the product of the failure of interference which occurs outside of conscious control (Edwards et al., 2012) and is supported by a wide range of neuroimaging studies which have revealed alterations in brain regions associated with sensory processing, motor control and emotion regulation (Aybek & Vuilleumeir, 2016; Hassa et al., 2021; Sojka et al., 2019; Sojka et al., 2024). There is evidence of psychological factors which are accounted for in this model, and factors that may contribute to alterations in prior beliefs and expectations, leading to increased susceptibility to prediction errors. Further, this model considers that FND symptoms can fluctuate in response to changes in attention, mood or context, which is consistent with the Bayesian model's emphasis on the

dynamic interaction between prior beliefs and sensory evidence. In therapeutic approaches, this model has been highlighted and influenced, particularly in, for example, the development of positive clinical diagnostic tools like Hoover's Sign (Edwards et al., 2020; Lidstone et al., 2020; Stone et al., 2020).

1.4.4 Other models and comparisons

Whilst previous aetiological understandings of FND relied upon simple trauma-focused explanations of a physical manifestation of psychological distress, neurobiological evidence has given rise to many other neurobiological models of FND. Voon et al. (2011) proposes the neurobiological model, which considers the aetiology of FND to reside in increased emotional arousal at symptom onset and a previously mapped conversion representation either at the onset or prior to symptom development, drawing upon their consistent findings of amygdala involvement in symptomology. They also draw support for their theory from research showing abnormal connectivity between limbic structures and supplementary motor area (Voon et al., 2010) and findings of higher activation of the right amygdala, left anterior insula and bilateral posterior cingulate (Voon et al., 2010b). Kozlowska et al. (2012) have proposed a neurobiological stress-based model of FND as a result of their work with children and consider that dissociation illness, injury, emotional distress, and trauma could lend to cortical arousal, abnormalities in brain function and connectivity. The authors suggest that FND is a result of a defensive state in which the brain is responding to cortical arousal and that the basal ganglia, midbrain and brain all engage in reflective behaviours (Kozlowska et al., 2012). Recently, Fobian and Elliot (2019) proposed an integrated summary model which aimed to consider the complexity of FND and integrate contemporary cognitive and neurobiological understandings and recent research in a model which was easily understood by patients. Whilst considering a wide range of literature and theory the model does contain a great emphasis on elements like "sick roles" and "health scaffolds" which are not welcomed insights by the patient community.

Given the wide range of symptoms including motor, sensory and cognitive symptoms, the heterogeneity of these suggests that a that a single mechanism, be that conversion or cognitive, may not adequately explain the diverse manifestations of FND. Whilst it is known that the functioning of the brain is subject to individual differences as its functioning is based upon our own experiences, this alone does not explain why FND symptoms vary and why individuals with FND suffer from alterations in symptom profiles and have slump-crash reactions (whereby symptoms can fluctuate sometimes without known cause or explanation). Theories often focus on a singular mechanism and sometimes neglect the complex interplay

between cognitive factors, internal (emotional or psychological) states, biological and environmental influences. There is a strong body of evidence that implicates a key psychological construct, dissociation, which has not been considered in its entirety in contemporary models of FND and is explored in greater depth throughout this thesis. Physical treatments, such as physiotherapy, graded motor imagery, transcranial magnetic stimulation (TMS), and neuromodulation techniques, have been shown to support recovery of FND symptoms, suggesting a physical component to the disorder – one which either has been overlooked or which remains elusive owing to current limitations of neuroimaging. Evidence of underpinning biological mechanisms is critical in adequately comprehending FND.

1.5 Stigma

Despite the absence of a suitable disease explanation, people with FND are frequently disabled and distressed (Carson et al., 2011) likely owing to a multitude of factors, including the unknown aetiology and neurobiology of FND, stigmatisation associated with the condition (Carson, 2016), unknown illness narratives (Nettleton, 2006) and a lack of treatment options (Stone et al., 2010) amongst other factors. Socio-political influences have greatly influenced understandings of the condition and definitions throughout history, yet arguably, medical stigma remains a great influence in FND and lends to adverse views of patients with the condition. The history of FND certainly contributes to this stigma and perpetuates myths of its legitimacy and where to place blame.

FND is a condition that poses significant challenges to healthcare professionals (HCPs). Studies have shown that HCPs exhibit varying, negative attitudes towards FND, with uncertainty and fear regarding diagnosis and treatment being common themes (Barnett et al., 2022; Begley et al., 2023; Evans & Evans, 2010; Kanaan et al., 2011; Marotta et al., 2021; Tinazzi et al., 2022). A study from 2010 found that neurologists rated FND as the condition that they least liked to treat among 20 common neurological disorders (Evans & Evans, 2010). Furthermore, a large proportion of HCPs express scepticism about the legitimacy of FND, often associating it with malingering, feigning, and manipulation (Barnett et al., 2022; Kanaan et al., 2011; Lehn et al., 2019; Tinazzi et al., 2022; Vance et al., 2024). Such negative attitudes may manifest in clinical interactions, leaving many people living with FND feeling unsupported (Dosanjh et al., 2021) and questioning of the diagnostic legitimacy of FND which can in turn exacerbate the illness and lend to a continued search for answers.

Limited formal training on FND management may contribute to these negative attitudes (de Liège et al., 2022; Stone et al., 2020). It is crucial to note that HCPs' attitudes can influence clinical decision-making, such as writing letters of support for patients or decisions to prescribe medications or psychological therapy (Drake et al., 2018; Schäfer et al., 2016) and that these attitudes continue to shape general population and wider medical sector views of the condition. Previous studies examining clinician attitudes towards FND have primarily focused on explicit attitudes, which refer to conscious and openly expressed opinions obtained through surveys or qualitative interviews. However, this approach fails to account for potential implicit biases, which involve less awareness and unintentional responses. Research in other medical conditions has shown that these implicit attitudes can influence both treatment decisions and patient health outcomes (Hall et al., 2015; Sereno et al., 2022). Recent research into FND shows that many HPCs hold implicit uncertainty regarding the legitimacy of FND and that such attitudes influence referral to other treatments limiting potential resources of support for those diagnosed (Begley et al., 2023). Moreover, it has been observed that implicit and explicit attitudes have different patterns of relationship with treatment decisions. Therefore, it is essential to consider both implicit and explicit attitudes towards FND to ensure that individuals living with FND receive appropriate care and support.

1.6 Triggers

Throughout the history of the conceptualisation of FND, a central focus has been on the initial 'trigger' – the predisposing event, situation or sometimes trauma (be that biological, physical or psychological) which has led to the beginning of FND (Stone et al., 2020; Fobian & Elliot, 2019). Such views continue to dominate practice, and as such, patients are medically traumatised whilst professionals aim to seek to find a trauma from which the illness stemmed. Whilst this search may be beneficial and allude to some answers, understanding how and why symptoms are maintained is a much more pressing concern. After the initial attack, when symptoms settle into more rhythmic patterns and the condition becomes chronic (Hallett et al., 2022). A range of predisposing factors including adverse life events (ALEs), viral infection, physical injury and combinations of these with emotional, psychological, and sensory processing deficits, burnout, stress or genetic vulnerabilities have been proposed (Millman et al., 2023; Ranford et al., 2020; Keynejad et al., 2019; Vanini et al., 2024). However, events like painful injury, viral infection and psychological and physical illness are almost universal

occurrences which do not result in FND for the vast majority of people who experience them (Parees et al., 2012). FND research is progressing from preliminary trauma enquiries and as a construct of evolutionary survival, particularly when we consider evolving understandings of the nature of trauma and that symptoms produced by FND are ineffective from a survival perspective.

FND, and FND attacks in particular, may be perpetuated by one or more of its own symptoms. In short, that FND could be a response to itself. Some theories suggest that after the initial trigger or impetus, subsequent symptoms may arise similarly, such as a series of self-perpetuating internal drives (or a positive feedback loop) that bind the symptoms into their own circulatory ineffective system. FND symptoms long outlast the provoking or triggering stimulus and are protracted beyond any reasonable adaptive or emotional response or function. In order to fully appreciate this concept, we should therefore shift our focus in research. Change can only occur in understanding and mapping the changes FND has resulted in – the maintenance symptoms or perpetuating symptoms, which perpetuate the illness and result in continual attacks and underlying constant symptomology. Whilst the triggers may be important, they can only be important in the context of their potential relationship to the maintenance symptoms and the potential biological changes that these resulted in, which enable the illness to continue. Research has begun to identify many possible perpetuating factors including Alexithymia, dissociative tendencies, emotional distress, and physical symptom burden (Millman et al., 2023) and rather than considering these as triggering symptoms the current thesis considers these as potential perpetuating factors in FND which could robustly account for variations in symptom clusters and fluctuations in symptoms. As an underlying mechanism in FND the current thesis explores dissociation and inflammation as core constructs and elaborates on these ideas further in Chapters 2 and 3.

1.7 Symptom-constellations in FND

Symptoms of FND are often listed and described as if they were unrelated to one another and occur at random. However, theoretical models presume that there is an underlying mechanism which somehow shifts to present different symptoms and variation of symptoms within this patient group. In clinical practice and community work, there are reports of symptom clusters occurring with some consistency and in relation to the predisposing (or

triggering) event. For example, those who report a physical event at the onset of the development of FND seem to show correlates with subsequent symptomology i.e. painful limb injuries are reported commonly prior to the onset of FND and the same limbs affected in functional dystonia (van Rooijen et al., 2011). Panic attacks, events of emotive significance and events which induce dissociation are commonly reported prior to the onset of functional seizures (Goldstein & Mellers, 2019). These accounts are suggestive of a relationship between initial triggers and subsequent symptomology though this has never been statistically explored. Equally, the trajectory of the illness can change. Someone who is 'in remission' may seemingly suddenly have incidents of paralysis or further long-term impacts. There are, therefore, two relationships that need to be considered: i) the relationship between symptoms and potential symptom clusters and ii) the relationship between symptom clusters, if these do exist, which may denote separate types of FND and their causes.

Chaos theory could be used to understand complex dynamic systems like that of the brain and nervous system in particular when the normal rules of the nervous system are paradoxical, as they appear to be in FND. We have an assumption that the brain and nervous system will prescribe a common set of rules and notions. But if this is true, and we view FND as a dysfunction – a breaking of these rules of 'normal', 'healthy' functioning, then we must ask why. The brain, of course, prioritises efficiency, survival, and protection of the organism, which does not align with the production of FND symptoms; FND represents chaos in this normal functioning. Conditions like Parkinson's (Toro et al., 1999; Yulmetyev et al., 2006) and Migraine (Kernick, 2005) are often thought to represent "an organised chaos", and the same could be said of FND. FND, in particular, is characterised by this chaos, which can manifest in various ways, including uncertainty, instability, intensity and flux of symptoms (Arbuthnott, 2020; Canna & Seligman, 2020; Barnett et al., 2022). As a result, those with FND may experience periods of disorder and unsettled states and, even in moments of relative stability may be left with a general "feeling of the disorder". There may be some periods of settling of symptoms or, for the lucky few, periods of "health". Nevertheless, there is always gravitation toward a stability of health or that of illness. While Chaos theory is not commonly applied to healthcare, it can be useful in understanding the complex dynamics of the body and nervous system and the interaction between these and other factors. FND can be viewed as a complex and dynamic disorder of neural behaviour, one which affects the regulation of the body's autonomic nervous system. Patients with FND may experience rapid imbalances and overcompensations due to even the slightest stressors, which can pull the ANS into a state of

chaos. Ultimately, FND may act as (in Chaos theory terms) a "strange attractor," drawing the body's systems away from equilibrium and into a state of disorder and into chaos.

Consideration of the many symptoms which may present in FND shows us that a single symptom cannot enable a thorough understanding of the entire condition and underlying mechanisms influencing symptoms. A rule that needs to apply not only to clinical practice but also to empirical research. FND is an aggregate of innumerable components, and whilst highly variable, it likely operates within a framework of a general pattern. Chapter 5 follows an investigation into a single multifaceted phenomenon, dissociation, which has long been overlooked in FND but is also variable in nature and could explain the chaotic nature of FND symptoms. Chapter 6 investigates the role of the potential pattern which may exist between symptoms, triggers and potential clusters for the condition. There are, however, a surprising number of symptoms which literature has overlooked, including altered sleep (either prolonged or a lack thereof), tinnitus, migraine, sensory issues, migraine, and the vividness of dreams) and the role of dissociative experiences across a range of mechanisms. In Chapter 6, an empirical study is presented that explores if symptom clusters exist, which include the less 'obvious' FND symptoms, and if these hold a relationship with predisposing and perpetuating factors.

1.8 Chapter summary and outline of subsequent chapters

This chapter has defined FND and considers its conceptualisation in relation to models of aetiology with support from empirical research and the historical perspectives and current challenges and controversies within the field. The evidence suggests that contemporary models can still not account fully for the onset of symptoms and that FND is a multifaceted and complex condition; thus, it is essential to continually revisit and revise conceptualisations and understanding of the psychological and biological mechanisms which underpin it. Current diagnostic tools are lacking in such advancements, and discrepancies between them and discrepancies of their outlook in light of recent empirical evidence suggest that these are not reliable in their considerations of FND, often adding further conceptual confusion. Chapter 1 has also emphasised the need to identify subtypes and predisposing factors and critical considerations that should be considered in theoretical models, including dissociation as a prominent symptom. Several models have been proposed to understand the aetiology of FND,

such as the cognitive-behavioural model, the trauma model, and Bayesian models. The symptom presentation of FND is diverse but these symptoms could be further classified into different clusters in advancements to contemporary theory and consider FND in light of chaos theory, which would view FND symptoms as the result of complex interactions between multiple factors.

The overall aim of this thesis is to contribute toward knowledge of FND and elucidate biopsychosocial markers for the condition which could reduce stigma and lead toward comprehensive treatment approaches or biological markers for diagnosis. The thesis aims to encapsulate a biopsychosocial approach and chaos theory to explore symptom profiles and key constructs like dissociation, brain function and inflammation in FND through a combination of self-report, behavioural, neurobiological and psychological measures. The aim is to also investigate relationships between these constructs to develop a comprehensive, holistic view of the potential underlying relationships between these in a mind-body holistic paradigm. A summary of the remaining chapter aims is outlined below:

- **Chapter 2**: A theoretical chapter providing an overview of the literature on psychological constructs and correlates in FND. In particular, this chapter considers the need to focus on dissociation as a prominent and defining feature across FND subtypes and symptom clusters.
- **Chapter 3**: A theoretical chapter providing an overview of the biological and neuroimaging evidence in FND and the methods of investigation used throughout this thesis, including electroencephalography (EEG) and inflammation (through phlebotomy measures).
- **Chapter 4:** Thesis aims and overview in their entirety and as informed by previous literature reviews.
- **Chapter 5**: The first empirical chapter provides primary investigations into the role of dissociation in FND and presents research findings to allude to a necessity to consider this throughout subsequent investigations.
- **Chapter 6**: Presents secondary empirical investigations into the role of dissociation in FND and analysis of latent class analysis (LCA) in investigating potential symptom clusters of FND in relation to predisposing (triggers) and perpetuating (dissociation) factors.
- **Chapter 7:** Presents an empirical multimodal study which explores inflammation in FND and combined analysis of dissociation and EEG resting state data.

- **Chapter 8**: This final chapter synthesises and discusses the thesis's overall findings as they relate to the core aims and theories of dissociation, brain function, and inflammation in FND.

Chapter 2: Psychological correlates of FND

2.1 Chapter introduction

In Chapter 1, conceptual understandings of FND were described along with a current understanding of the condition; nuances in its presentation were also alluded to. Contemporary models of FND have shifted away from longstanding psychodynamic theories or trauma-focused models towards models which emphasise dysfunction of higher-order cognitive processes and consider several aetiological risk factors, beyond psychological trauma (Edwards et al., 2023; Teodoro et al., 2018; van Den Bergh et al., 2017). Such models state that there is a complex interplay in FND between genetic, developmental, psychosocial and environmental factors, which accumulate as "multi-hits" to trigger and maintain cognitive, sensorimotor and emotional dysfunction underpinning FND symptoms (Pick et al., 2018; Pun et al., 2020). The relative extent to which each element plays a role is greatly debated (Butler et al., 2021; Ludwig et al., 2018; Jungilligens et al., 2022;). Throughout Chapter 2, consideration is given to alternative ideas for the role of trauma, affect, and coping in FND. Chapter 2 also introduces dissociation, alluded to in some models and explored throughout the current thesis as critical constructs in FND.

2.2 The role of trauma

The role of trauma and stress in FND remains controversial in research and practice (Keynejad et al., 2019). Emphasis on the role of trauma in FND stems from the historical conceptualisations of FND as a stress-related condition. As a result, many researchers have explored trauma as being a predisposing factor for the development of FND symptoms; some (Jungilligens et al., 2022; Ludwig et al., 2018; Perez et al., 2017; Roelofs et al., 2002; 2005; Selkirk et al., 2008; Spinhoven et al., 2004; Stone et al., 2004), but not all (Blanco et al., 2023; Reuber, 2007) studies have found that adverse life experiences (ALEs, e.g., sexual abuse) are higher in those with FND, and claim that trauma is an antecedent to the development of FND. Discrepancies in findings might result from differences in methodological approaches (e.g., reliance on recruitment through neurological and/or psychiatric clinics), possibly indicating the existence of FND subtypes (Jungilligens et al., 2022) that differ in aetiology, and/or alternative

triggers. That is, trauma may be one factor in a complex interplay between several possible environmental, psychological, social and genetic determinants (Keynejad et al., 2019).

There remains a question of how to best conceptualise these findings of adverse life events (ALEs) and trauma in more contemporary understandings of FND (Kanaan & Craig, 2019). The psychogenic model of FND has been widely criticised (see Edwards et al., 2013; Stone & Edwards, 2011; Stone et al., 2011) for its simplistic assumptions and lack of reflection on the patient experience of the illness, leading to a reduction in diagnostic importance of ALEs in DSM-5. Downgrading the presence of a psychological stressor from an essential to a supportive criterion (Espay et al., 2009) is further supported by findings that trauma represents a susceptibility factor for many non-communicable diseases, including neurological and psychiatric illnesses (Roelofs et al., 2005; Sharpe & Faye, 2006). Trauma as a risk factor is not specific to or sufficient for the onset of FND (Nicholson et al., 2020), and consideration should be given to the wide range of risk factors that the literature indicates. A range of nonspecific factors and complex pathways of predisposing traumatic experience can be linked to precipitating and perpetuating experiences in FND and its symptomology (Reuber et al., 2009). These include affect, emotional dysregulation and stress (Janiri et al., 2021; Jungilligens et al., 2022). The presence of psychological stressors can only be identified in a small proportion of patients (Binzer, 1997), and often, these occur years prior to the onset of symptoms (Roelofs et al., 2002). Moreover, patients with FND more commonly report a physical event at the onset of symptoms (Reuber et al., 2002). Nonetheless, findings of psychological trauma may represent a risk factor for a proportion of those diagnosed but likely alongside other risk factors in multi-hit hypotheses (Ludwig et al., 2018; Stone et al., 2004).

There could be differences according to symptom clusters and ambiguous current and possible (i.e., only theorised) types of FND. Stone et al., (2004) report that those with Functional Seizures show particularly heightened rates of trauma within 12 months of symptom onset. Another study found that those with Functional Seizures had significantly more prevalent ALEs than those with epilepsy and that they showed higher levels of stress-related disease and current rumination (Tojek et al., 2000). However, in both cases, the authors advised caution in the interpretation of their results. Stone et al.'s (2004) findings, for example, did not extend to those with other types of FND (such as motor symptoms). Thus, findings of heightened trauma and adverse life events may not extend to all symptom clusters in FND. Functional seizures may in themselves relate to a larger pattern of somatic symptom responses to a wide range of negative events, including stress in adulthood and stress across the lifespan.

Such findings raise questions about the helpfulness of a diagnostic category which assumes a singular underlying aetiological mechanism and unified treatment modalities. Rather it is suggestive of different causal pathways in the development of different subtypes of FND. Further, it could be argued that the patient's voice is being lost as many report feeling stigma from healthcare professionals who search for trauma when there is no trauma apparent. Indeed, the illness itself, with the changes and chaos it creates, is traumatic.

Additional research is clearly needed to understand the intersection of disease mechanisms, aetiological factors in FND and treatment influence within the context of the biopsychosocial and cognitive neuronal models of FND. This should also consider spiritual and cultural influences that could influence experiences of trauma (Raghavan & Sandanapitchai, 2020), the role of influence on neuronal networks and subsequent symptomology, and the bidirectional relationship between these. FND symptoms themselves produce trauma, as shown in other health conditions (Griesbach et al., 2018; Katrinli et al., 2022;), but not directly studied in FND. In FND, there is a need to understand psychological risk factors of brain circuity and subsequent illness outcomes. However, there is also a need to contextualise a range of mediating and modulating factors, including genetic/epigenetic factors, developmental trajectories (including critical periods), gene-environment interactions and an attempt to explain better a range of risk factors and later life development of FND (Perez et al., 2021). Very little is known about biological stress regulation generally and how it may impact predisposing biological and psychological risk factors in a range of illnesses, particularly FND. There are findings of hypothalamic-pituitary-adrenal axis dysfunction and postulated relationships to preceding trauma and ALES, brain anatomical/functional changes evidenced by neurochemical indicators like cortisol (Weber et al., 2023).

2.3 Role of emotion

Emotions are temporarily fixed states as opposed to the longer-term construct of mood; as such, this chapter considers these as separate constructs for discussion. Like trauma, the role of emotion (particularly those of negative valence) in FND has long been a research interest which aligns with historical conceptions of FND as hysterical conversion. Psychodynamic theories (e.g., as proposed by Breuer & Freud, 1893), Sojka et al., (2018) emphasise the importance of emotions in FND pathology drawing upon evidence of higher rates of mood

disorders and health anxieties. However, current empirical evidence suggests that historical and precipitating stressors are neither necessary nor sufficient to cause the disorder (Keynejad et al., 2019). The role of emotion is more complex than this simple linear assumption in its role in the pathology and development of symptoms in FND.

Rather than being considered as a cause or triggering factor in the development of FND, as the above works indicate, emotional dysfunction in FND could be viewed as a symptom or byproduct of underlying pathology. The known pathophysiology of FND involves dysfunction within various brain circuits, which affect constructs like emotional processing, interoception and attention (Drane et al., 2021). Kozlowska et al. (2018) highlighted that patients with FND show activation of multiple components of the stress system, including the hypothalamic-pituitary-adrenal axis, autonomic nervous system and brain regions involved in both arousal and emotion processing. Findings here were suggestive of the immune-inflammatory component of the stress system, which may also be activated in those who develop FND. At a circuit level, interrelated emotional processing functions map onto salience and other limbic and paralimbic circuits, e.g. ventromedial and orbitofrontal prefrontal cortex, parahippocampus and hippocampus. Heightened emotional reactivity and issues with arousal could be attributed to symptoms of FND as a result of increased bottom-up amygdala and periaqueductal grey PAG activations and alterations in functional connectivity associated with the hypothalamus with is associated with detecting and responding to homeostatic demands (Aybek et al., 2014; Lanius et al., 2010; Voon et al., 2010).

Unlike in other disorders where symptoms may take hold of a person mid-excitement (psychological or physical) or immediately after a peak of excitement, FND symptoms act with greater sporadicity. Some symptoms of FND have parallels to migraine reactions, the fainting spelling in narcolepsy and cataplexy, the freezing exhibited in Parkinson's patients or fainting and swooning spells associated with vasovagal syncope. In such cases, however, the literature suggests symptoms arise as a result of proactive emotions whereby excitement of the neurological system lends to extreme kinaesthetic output. Emotions which hypo- (rather than hyper) activate the nervous system do not typically lend to the symptoms seen here nor to seizures. Yet literature continues to consider more negative emotions in the development of FND. FND symptoms are sometimes linked to a specific trigger (Geroin et al., 2022; Millman et al., 2024; Stone et al., 2020) and there can be clear links between the nature of the physical precipitant and the resulting functional symptom (Stone et al., 2009); however, typically, these triggers are more likely to lead to hypoactivation of the nervous system including stress

responses, mood, dissociation, pain, fatigue and inflammatory responses. Sometimes, patients report no identifiable trigger at all (Stone et al., 2020). Despite knowledge of the role of emotions which excite or lend to hyperarousal of the nervous system, the rules are somewhat disregarded in FND. There is evidence of emotion regulation and amplification of functional symptoms during negatively valanced or psychologically threatening mood states e.g. panic or shame, deficits in emotional awareness (such as psychological arousal in the absence of emotional arousal and alexithymia and aberrant salient processing particularly in the induction or worsening of FND symptoms (Pick et al., 2018).

Interoception, the capacity to identify sensations arising from the body is also suggested to play a role in FND and has been associated with the ability to recognise and understand emotions (Damasio, 2006; Zamariola et al., 2019). Research suggests that interoceptive abilities relate to emotion regulation, with higher interoceptive abilities indicative of more robust emotion regulation (Kever et al., 2015; Pollatos et al., 2015; Werner et al., 2010). In FND, the processing of emotions is thought to be dysfunctional, but this is indicative of the role of affective dysregulation and impaired cognitive control in the pathology of the disorder and may be reflective of inefficient voluntary emotion regulation strategies (Sojka et al., 2019). Individuals with FND may have abnormalities in interoception, and this difficulty in processing emotion leads to difficulties in the identification of emotions; an understanding of brain mechanisms underpinning the interpretation of physiological signals is crucial in understanding the emotional experiences in those with FND (Jungilligens et al., 2022; Williams et al., 2021). However, recognition needs to be given to the multifaceted, interconnected and complex relationship between emotions and FND as this is not a simple linear relationship. Consideration needs to be given to triggering factors, but also of interoceptive awareness and cognitive dysfunction, and it seems these could be indicative of underlying brain and neurobiological pathology in FND.

2.4 Mood

In comparison to emotion, mood describes a general background state, which is longer in duration and differs from emotion in intentionality, anatomy, intensity, awareness and function (Beedie et al., 2005). Mood disorders occur when there is a sustained abnormality of a person's mood and are chronic lifelong disorders of altered mood states, symptom clusters of which are used to identify type and treatment modality (Grof, 2002; Marneros, 2009; Price &

Drevets, 2010). Several studies report a high incidence of co-occurring mood and/or psychiatric disorders, including poor concentration, low mood, anxiety, panic, dissociative phenomena and post-traumatic stress symptoms as well as increased pain and sleep disturbances among other non-core neurological aliments (Akyüz et al., 2017; Butler et al., 2021; Pick et al., 2020; Perez et al., 2021; Şar et al., 2004). These studies frequently reported that co-occurring symptoms worsen clinical outcomes and are as disabling as the core features of FND (Gelauff et al., 2014; Glass et al., 2018; Nicholson et al., 2020) and worsen quality of life (LaFrance et al., 2009; Jones et al., 2016). Indeed, co-occurring physical and mental health diagnoses are considered to be the norm rather than the expected in FND (Nicholson et al., 2020). This could reflect shared risk factors such as biopsychosocial mechanisms, including trauma and other precipitating events. However, not all research has demonstrated a link between FND and co-occurring disorders of mood with some finding low rates in FND cohorts (Fobian & Elliott, 2019; van der Hoeven et al., 2015). It should also be acknowledged that other neurological disorders (e.g., Multiple Sclerosis, Epilepsy, Fibromyalgia and Parkinson's) are also associated with high levels of anxiety, depression and dissociation (Bulloch et al., 2015; Davies et al., 2001; Karatzias et al., 2017). In other disorders of the brain or neurological deficits, mood disorders are considered to be a result of shared neural circuits implicated, for example in Traumatic Brain Injury (TBI) it is recognised that the pathophysiology of mood disorders may pertain to the injury itself and the associated structural and functional changes linking areas of the brain associated with emotional processing (Jorge, 2015). There are individual differences in the amygdala and PAG volumes in FND, which positively correlate with symptoms of ill mental health, anxiety and disturbances in affect across FND subtypes (Perez et al., 2017).

Few studies include neurological controls alongside healthy comparisons, which can limit the interpretation of findings being specific to FND. That is, such designs are less able to distinguish the impact of having a long-term illness on mood (e.g., suffering and debilitating effects, impact on social contact and recreation etc). Other factors influencing mood in FND include medical gaslighting (Merone et al., 2022; Pierce & Albert, 2022), social support (Ospina et al., 2019), cultural context, meaning (Canna & Seligman, 2020), stigma (Foley et al., 2024; MacDuffie et al., 2021) and health status (Matin et al., 2017; Perez et al., 2017; Scott et al., 2019), to name a few. Also, given that those with FND (and other neurological conditions) are more than three times as likely to engage in mental health treatment than their control counterparts (Fargo et al., 2004), it is more likely that mood symptoms, if present, will be detected. Mood cognition and emotional responsivity are also affected by psychotropic

medications, often prescribed in FND, which will impact incidence. Thus, a simple linear relationship between mood disorders triggering FND onset is unlikely (Keynejad et al., 2019), and bidirectional relationships between mood and FND also need to be considered. As is later discussed in Chapter 3, a shared mechanism could be the presence of inflammation. The broader literature implicates depression in exacerbating inflammation and dissociative experiences (Beurel et al., 2020; Dantzer, 2012; Pike & Irwin, 2006; Powers et al., 2019). This could also perpetuate a cyclical relationship between mood and FND symptoms, particularly if inflammation also underpins FND and dissociation (for full discussion see 2.6 and 3.5).

Disruption to emotional states and mood disorders could be underpinned by impairments in interoception and Alexithymia. Whilst dysfunction of interoception refers to the disruptions to a sense of the internal state of the body with sensations associated with emotional arousal, Alexithymia is characterised more broadly by difficulties in the identification, description and expression of one's own (or sometimes others') emotions and mood states (Herbert et al., 2011; Kauhanen et al., 1993; Mattila et al., 2009). Thus, in Alexithymia, whilst physiological sensations of emotion (like heart rate, hunger, thirst or emotional arousal) may be felt, these are found to be challenging to identify, recognise, describe and express. Alexithymia has been associated with poor health-related quality of life and interpersonal and economic disadvantages (Kauhanen et al., 1993). Alexithymia is significantly more common in those with FND compared to healthy controls and other illness control groups (Demartini et al., 2014; Gulpek et al., 2014; Kaplan et al., 2013; Steffen et al., 2015). This difficulty in identifying feelings also entails externally oriented thinking and limited imaginal capacity (Williams & Gotham, 2021) and has previously been widely studied in the context of autism spectrum disorders (ASD). More recently however links have been established between FND and neurodiversity (Cole et al., 2023; Nisticòet al., 2022) with evidence of high rates of autistic traits in those with FND (Cole et al., 2023) and high rates of Alexithymia have been identified in FND (van Dijl et al., 2024). There is some evidence to suggest that emotional processing is more commonly associated with Functional Seizures than more general FND types (Bewley et al., 2005; Kaplan et al., 2013; Urbanek et al., 2014) researchers recognise that this may be owing to a multitude of factors and direct comparisons between subgroups have not yet been conducted. Evidence suggests that FND is associated with difficulties in processing emotion-related stimuli and both emotional and mood experiences. This, however, could be viewed as a result of the underpinning neurobiological

mechanisms which occur as a result of the development of FND, rather than a triggering factor, but could be a determining factor in chronic mood states.

2.5 Other Psychological States

Some research has proposed that FND symptoms, particularly fluctuations in chronic states, are an adaptive coping mechanism in response to mood disruption or trauma (e.g., Brown, 2016; Cretton et al., 2019). FND itself should not be proposed as being a psychological state of affect in which there is a perceived reward for the production of symptoms, as this chapter has suggested the evidence for this position is weak and likely a result of historical misconceptions of the disorder. Instead, diverse and understudied FND symptoms, including allergic reactions, complex migraine and other symptoms which fluctuate, may represent cellular, localised sensitivities. These are signs of different mechanisms of manifestations of the brain and body's difficulties in adaption as opposed to a commentary on the lack of resilience to psychological turbulence. Sensitivities to temperature, new allergic reactions and other factors show an inability to process particular sensory information in FND (Matin et al., 2017; Ranford et al., 2020; Stephen et al., 2021) and represent manifestations of difficulty in adaptions of different areas of function. Simply, the brain and body are not communicating well, and neuronal dysfunction as a result of separation of functions that are usually intrinsic are not able to adapt to environmental changes and add another layer of complexity to FND.

On the topics of coping, Sydney Smith (1844) once wrote in relation to chronic illness, "…I am taking all proper care of myself which consists in eating nothing that I like, and doing nothing that I wish" (p. 508–509). Being chronically unwell adjusts life's structure and function, which is often seen in those with FND (Graham et al., 2018; Staton et al., 2024); whole lives and livelihoods change (Stewart et al., 2004). Some patients fixate on the strategies and techniques that will make them better, make small incremental changes to their symptoms and come to accept that living with a diagnosis of FND takes great adaption (Arbuthnott, 2020) as does psychosocial adaption to a wide range of chronic illness and disability (Livneh, 2001). Health anxieties or quests for answers are sometimes viewed in FND as a response to disrupted mood or health anxiety, as opposed to a primal instinct to support recovery. Whilst there is indeed a need (sometimes) to allow the symptoms to take over, it is not through conscious choice to be ill. Sydney Smith (1844) also wrote in the same set of letters to Lady Grey on the power of connection between suffers of similar fates and illnesses and on the power of this social support with others who are seemingly in an impossible state. Rather than an inability to

cope, this thesis proposes that FND is a result of dysconnectivity across a number of mechanistic traits like inflammation, dissociation and neural networks and that psychological distress is a byproduct of this dysconnectivity and that historical connotations have influenced the progression of understanding of this disorder. Further recognition needs to be given to elements which could influence mood and emotional states, including social factors (e.g., stigma, support, medical gaslighting) and psychobiological states (e.g., inflammation, dissociation and health status), as these may act as social, psychological and biological antecedents of mood states and psychological health.

2.6 Dissociation

Dissociation, in its broadest sense, describes a loss of integration of typically integrated cognitive functions. Conceptualisations of dissociation usually consider a loss of awareness of cognitive or physical processes and represent a state of altered conscious awareness (Goldberg, 2020; Lanius, 2015). Symptoms may manifest as a feeling of disconnectedness from memory, the self (depersonalisation), external stimuli or surroundings (derealisation), loss of bodily sensation voluntary control or a loss of self/identity (Cardeña & Carlson, 2011; Dell, 2002; Medform et al., 2003; Romero-López, 2016). Dissociation, therefore, can be defined as a loss of control, awareness or a lack of integration of processes that are normally integrated (Dell, 2006; Nijenhuis & Van der Hart, 2011). Whilst previously considered to be a concept more closely related to trauma responses, conceptualisations have broadened to include more precise definitions and conceptual integration of psychological theory and a broader range of psychological symptoms, states and cognitive processes (Nejenhuis & Van Der Hart, 2011; Sar & Ozturk, 2013).

When recalling life events with escape or dissociative potential, people with FND have dorsolateral prefrontal cortex (dlPFC) activity and lower left hippocampal activity, with increased activity in the right Sensory Motor Area (SMA) and temporoparietal junction (TPJ), particularly when recalling traumatic life events (Aybek et al., 2015). However, these patterns of activity differ from those seen in healthy controls, where trauma recall typically involves balanced hippocampal-prefrontal engagement, crucial for integrating emotional and contextual memory. In contrast, individuals with FND show a disconnection between emotional processing and motor control networks with exaggerated engagement of motor and sensorimotor integration areas (SMA, TPJ) at the expense of hippocampal-mediated

contextualisation. The TPJ, known for its role in self-referential processing and body schema, shows greater activity in FND, possibly reflecting disrupted sensory integration and a failure to reconcile bodily experiences with conscious awareness. This suggests that, rather than trauma being merely re-experienced, there is a fundamental alternation in the way emotional and bodily signals are integrated and could relate to changes in other cognitive domains, motor cognition and body schemata. The lack of ability to successfully integrate emotional and sensory experiences into a cohesive self-representation supports a role for dissociation rather than a direct expression of psychological trauma (Van den Bergh et al., 2017).

Conceptualisation and the history of progressive understandings of dissociation as a phenomenon have not been without controversy. Unitary models of dissociation, which have been dominant throughout the field, characterise dissociation as being produced by common psychological mechanisms and a breakdown of mental integration (Bernstein & Putnam, 1986; Dell, 2006). Through this lens, a wide range of phenomena, including confusion, depersonalisation/derealisation, intrusive thoughts or feelings, loss of control and voluntary action, identity confusion alternative or multiples, trance states, hypnotic susceptibility, attentional difficulties, memory issues and "medically unexplained symptoms" could be considered under dissociation (Cardeña & Spiegel, 1996). Yet it considers all these phenomena as being qualitatively similar, distinguishing differences by the amount, rather than type, of dissociative experiences. The unitary model informed DSM-IV definitions wherein dissociation is categorised by amount rather than category or type and led to the development of the dissociative experiences scale (DES; Bernstein & Putnam, 1986) which is widely used in research. However, the unitary model is based upon a definition of dissociation which obscures fundamental differences, which has implications in research, measurement and clinical practice where exploration of symptom type rather than overall amount could be more beneficial. This has led to an increased search for the identification of dissociation types (Brown, 2006; Schmidt & Vorberg, 2006; Schimmenti, 2018; Waller et al., 1996) and explorations of multifactorial measurements for dissociation (Briere et al., 2005; 2016; Holder, 2013). Discrepancies remain in literature of a consensus on this issue; this is further reflected in differences between major classification systems approaches, which can create further conceptual confusion for conditions like FND, which subsume many dissociative concepts.

Dissociative pathology has been studied across a range of psychological and neurological disorders including Schizophrenia (Bob & Mashour, 2011), Epilepsy (Medford, 2014), Multiple sclerosis (dissociative memory; Scarrabelotti & Carroll, 1999), affective disorders

(Lyssenko et al., 2018; Spiegel & Simeon, 2015), Obsessive-compulsive disorder (Soffer-Dudek, 2014), Post Traumatic Stress Disorder (PTSD; Armour et al., 2014) and a range of others (Lynn et al., 2019) as well as distinct personality traits (Kwapil et al., 2002; Nijenhuis et al., 2010). Investigation of the psychological manifestations of disorder has in part been influenced by the history of conceptualisation of dissociation and links to traumatic experiences (Nejihus & Van Der Hart, 2011). Whilst dissociative tendencies are considered to be natural responses to particular triggers like sleep deprivation or extreme fear, the conceptualisation of pathological dissociation should be considered across illnesses (Hunter et al., 2003; Medford et al., 2003; Ross et al., 1990) mainly as dissociation is an essential predictor across illness for poor treatment responses, high relapse and contributes toward likelihood of development of severe mental ill health, severe chronic symptoms and symptoms of dissociation are extremely disabling (Bailey & Brand, 2017; Cronin et al., 2014; Halvorsen et al., 2014; Spitzer et al., 2007; Thompson-Hollands et al., 2017). Dissociation as a symptom across neurological and neuropsychological illness is progressing our understanding of both conditions and the conceptualisation and impact of discussion; not only can dissociation be a risk factor for the development of illness, but it can also be viewed as a byproduct or symptom of the disorder (Campbell et al., 2023; Loewenstein, 2018). In whichever direction this is to be viewed, as either a predisposition to the development of chronic illness or as a byproduct or symptom of the illness itself, it is evident that additional symptoms from dissociation are chronic and disabling (Lyssenko et al., 2018; Medford et al., 2003). A lack of recognition of their importance and influence in chronic illness could further hinder those diagnosed.

A lesser discussed underlying symptom of FND is dissociative symptoms, and indeed, these are only notionally considered in theoretical frameworks of the condition. The history of the conceptualisation of dissociation does at times blend and morph into the history of FND, and the first clear notion of an association between the two is in the 19th century when Pierre Janet considered FND to be a product of functional lesions, a process underpinned by the concept of compartmentalisation. This process of compartmentalisation (Holmes et al., 2005) relates to the distinct conceptualisation of two different forms of dissociation phenomenology, and conceptualisation of this was not present at the time of Janet's writing (Brown, 2016; Holmes et al., 2005). Despite conceptual issues in both FND and dissociation, there is a large body of evidence that warrants consideration of a strong relationship between the two and the inclusion of dissociation in theoretical models.

Dissociation could be considered as an underlying mechanism or product of FND symptoms owing to the overlap of symptoms, characteristics and conceptualisation and the influence of dissociation on executive control (Osman et al., 2020). Dissociative symptoms are frequently reported in FND as demonstrated by meta-analyses by Campbell et al., (2023) and Lyseenko et al., (2018). Theoretically, this relationship supports many theoretical models of FND; for example, dissociation could emerge from ALEs, particularly those in childhood (Cromer et al., 2006) and thus supports trauma theories or theories of FND resulting from psychological distress (Fobian & Eliott, 2019). The compartmentalisation of dissociative experiences also could uphold theories of psychological distress, alexithymia, dysfunctional interoception and emotional dysregulation in FND, with evidence that over 48% of those with FND also meet the criteria for dissociative disorder (Akyüz et al., 2017). Previous research has found these issues to be comorbid in 47 – 51% of patients (Şar et al., 2004), and a relationship between dissociative tendencies and FND (van der Kruijs et al., 2012). Others have found that there is a significant correlation between psychological dissociation and the general psychopathology and personality disorders in those with FND, which provides further support for theories of this nature.

Evidence of dissociation is also implicated in neurobiological understandings of FND and could be considered as a missing component of models and a vital mechanism that underpins FND symptomology. Dissociation has been associated with cortical thickness in FND, and high rates of somatoform dissociation are linked to reduced left caudal anterior cingulate cortex cortical thickness (Perez et al., 2018). Emergence of findings of high rates of derealisation (detachment from surroundings) and depersonalisation (feelings of being outside one's self) are positively correlated with right lateral occipital cortical thickness which advances understandings of the neuropsychological contextualisation of dissociation in FND (Labate et al., 2012). Functional neuroimaging has found alterations in connectivity in those with functional seizures which correlated with dissociation measures (Van der Kruijs et al., 2012) and increased co-activation of resting-state networks in frontoparietal (e.g. orbitofrontal cortex), executive (cingulate and insular cortex), sensorimotor and default mode networks which also correlate with dissociation scores in Functional Seizures (van der Kruijs et al., 2012). Various psychological and cognitive features of investigation across FND subtypes have been shown to hold a correlational relationship with dissociation scores, including alexithymia, emotion dysregulation and cognitive distortions (del Rio-Casanova et al., 2018; Kienle et al., 2017, 2018; Pick et al., 2017; Williams et al., 2019). Findings from electroencephalography

(EEG) also explore connectivity within FND subtypes and some have found relationships between emotional regulation, connectivity and dissociation in FND (Kienle et al., 2018) others, though noting differences in connectivity particularly disruptions between frontal and posterior regions relative to controls, have not found associations between disruptions to connectivity and self-reported dissociation (Xue et al., 2013). Nevertheless, findings could support a rationale that deficits in attention in FND are a result of the disintegration of sensory, memory and motor functions related to dissociation (Levy & Behrman, 1970) and an extensive history of research supports that high levels of dissociative tendencies are significantly correlated with decreased neuropsychological availability and neuronal network dysfunction across many overlapping areas of FND symptomology including deficits of memory, attention, executive functioning and cognition (Guralnik et al., 2007; Osman et al., 2020; Özdemir et al., 2015; Price & Thompson, 2007).

Besides this, many other neural and cognitive correlates have been considered in traditional models but could be reconsidered under the framework of dissociation. For example, FND patients generally show the formation of abnormal inferences, and this lends to the adoption of fixed and sometimes exaggerated beliefs based on a limited set of information (e.g. jumping to conclusions; Finme et al., 2007) and such conclusions are in themselves limited because the processing of sensory data is also dysfunctional (Parees et al., 2012). This cognitive pattern could be integrative of cognitive processes akin to dissociation. There are also deficits in attention allocation (Edwards et al., 2012; van Poppelen et al., 2011), which have previously been considered under traditional theories (e.g. Edwards et al., 2012; Voon et al., 2011) but could be considered as manifestations of dissociation where disruptions of attentional networks lead to fragmented or impaired cognitive processing. Diminished integration of conscious and bodily emotional experiences, as shown by affective picture paradigms (Pick et al., 2018; Roberts et al., 2012) and heightened, maladaptive startle response (Seignourel et al., 2007) represent disconnect between emotional processing and bodily responses and disturbances in emotional regulation and arousal whereby startle responses show heightened sensitivity to sensory stimuli or difficulty in modulating emotional reactions, which are synonymous with conceptualisations of dissociation (Ebner-Priemer et al., 2005; Elsesser et al., 2008; Oathes & Ray, 2008; Sergerie et al., 2006).

Taken together, studies present a rather inconsistent picture regarding the presence of types of dissociation in FND. Dissociative symptoms are frequently reported in FND and a neurocognitive process; this could, in theory, underlie FND symptomology, which is reflective

of its categorisation in the ICD-11 where it is termed dissociative neurological symptom disorder (Brown et al., 2007; Brown & Reuber, 2016; WHO, 2019;). However, there is controversy at assuming that FND should sit alongside other dissociative disorders like dissociative identity disorder (DID). The conceptualisation of FND as a dissociative disorder, i.e. one in which dissociation is the core underlying mechanism, is not universally accepted and is not being proposed here. Instead, it is clear that patients with FND do have dissociative tendencies, and empirical evidence indicates that this is a gradual process caused by the generation of FND. This, too, is reflected in the DSM-5 classification of FND, and this is likely one of many underlying mechanisms of FND. Further investigations are needed between different FND symptom clusters or profiles and dissociation typology as well as the nature and role of dissociation in holistic models of FND. Evidence of dissociation in FND has often relied upon small samples and inconsistent measures, and there is a lack of consideration of the history and conceptualisation of dissociation and its component types.

2.7 Chapter Summary

Chapter 2 of this thesis focuses on the psychological correlates of Functional Neurological Disorder (FND) and aims to expand on the understanding of FND introduced in Chapter 1. Contemporary models of FND emphasize the dysfunction of higher-order cognitive processes and consider a range of factors, including genetics, developmental issues, psychosocial and environmental factors, and alterations in neurobiological functions. Chapter 2 delves deeper into the role of psychological correlates in the development and continuation of FND symptoms, including the controversial role of trauma. While some studies have found trauma to be a predisposing factor for the development of FND symptoms, others have not found such a link or have suggested that trauma may represent a subtype of FND triggered through complex mechanisms. Despite discrepancies in findings, adverse life experiences (ALEs) and trauma remain relevant to contemporary discussions. Furthermore, the role of emotion and emotional dysregulation as mediating factors between psychological stress and FND symptomology must also be considered. The chapter challenges the view of FND as a condition of coping. Whilst many other areas of psychological correlates in FND could not be explored in its entirety and the line between, for example, psychological and neurological correlates is challenging to frame, the chapter does include elements of consideration for the role of attention allocation, cognition and motor cognition throughout. Finally, the chapter considers the role of dissociation in FND, which is often overlooked in theoretical models and

which is a construct which contains many controversies in conceptualisation itself. However, its importance and overlap with FND symptomology cannot be underestimated. This core construct will be explored throughout the experimental chapters to follow. Overall, chapter 2 aims to underscore the need for a nuanced understanding of the psychological correlates of FND and the complex interplay of various factors in the development and maintenance of the disorder. Chapter 3 will go on to discuss the neurobiological correlates of FND in further refinement and enhancement of contemporary understandings of FND and in introducing further methodological insights utilised in the subsequent studies in this thesis.

Chapter 3: Neurobiological Substrates of FND

3.1. Chapter introduction

Chapter 1 outlines the progression of conceptualisation in FND; early conceptions of FND were integrative, forward-thinking, and considered FND to be a functional condition underpinned by mechanisms of altered function in the mind and body (Charcot, 1888). However, limitations in neuroscientific methodologies contributed to a progression of thought along trauma-based notions (Breuer & Frued, 1895; Janet, 1907). These theories are now largely discredited, though it is recognised that trauma is likely a factor but not the only one which contributes to the dysfunction seen in underpinning biological mechanisms and psychological correlates in FND (Nicholson et al., 2020). As the divide between neurology and psychology continually expanded throughout the 20th century, this was particularly determinantal to the progression of understanding of conditions situated between these two disciplines, including FND (Fend et al., 2020). Given this division and the high rates of diagnosis, the consequences within healthcare provisions and the personal burden experienced by individuals with FND, this has been deemed a "crisis" within the field and calls for action have been made (Edwards, 2019; Hallett, 2006; Keynejad et al., 2017; Nicholson et al., 2011).

Chapter 2 has conceptualised the significant strides in understanding the psychological correlates of FND, establishing a crucial role for contemporary psychological investigations. Chapter 3, on the other hand, takes a broader perspective, exploring the exciting advancements in understanding the neurobiological mechanisms of FND. A surge of investigations, informed by the biopsychosocial model, are advancing our understanding of FND using diverse neuroimaging and neuroendocrine methods (Baizabal-Carvallo et al., 2019; Bègue et al., 2019; Pick et al., 2019; Voon et al., 2016). Elucidating neurocognitive and neuropsychological mechanisms of FND has several advantages, including reducing stigma, developing biological diagnostic markers, and informing treatments. Chapter 3 aims to provide an overview of these advancements and highlight key findings in this field. It also explores current limitations and provides theoretical background for the empirical studies which follow.

3.2 Reconceptualising FND

Whilst Chapter 1 sets out recognised clinical definitions of FND, this alone does not fully encapsulate the full nature of this illness's complexity. The symptom profile of someone diagnosed with FND can change and alter over time. Based on clinical accounts and anecdotal observations, Nicholson et al., (2020) suggest symptoms can resolve and new ones develop in their place. However, this is yet to be supported by empirical evidence (Butler et al., 2021), and additionally, it is known that symptoms in FND are not always stable as people can experience 'attacks' of some symptoms. To further complicate this, some symptoms of FND, such as functional seizures or functional movement, are considered by some to represent distinct symptom subtypes (Ertan et al., 2022; Espay & Lang, 2015; Hingray et al., 2022; Perez & LaFrance, 2016; Rather & Cavanna, 2020). As such, FND can be characterised as a spectrum of symptoms, some of which operate continuously at lower functional levels but can include attacks which target higher functional levels. This is due to a continuous, hypo-alteration of homeostatic function, neuronal connectivity and reduced cognitive and sensory capacity interlaced. This hypo-alteration is likely interlaced with attacks which demonstrate hyperactivation (as seen by such as hypersensitivity, hyper-sensory arousal or, in the case of movement, attacks of tics or convulsions). Additionally, those with FND may have sudden spikes in ability, energy or other symptoms followed by crashes which may last for moments, weeks, months or even years (as was characterised as slump-crash reactions in previous chapters). The key, therefore, could be to stabilise the problematic internal systems, be it cognition, awareness, consciousnesses or physical energy levels/fatigue. This targeting the system that gives rise to the symptom(s) or that is causing the most detrimental impairment. Stabilisation could lead to symptom reduction, crash avoidance and improved overall symptom profile. This can only be done if the internal underlying mechanisms which lead to such systems becoming destabilised are elucidated and their role in symptom development is established.

3.2.2 FND as a neural network disorder

Exploration of neural networks has yielded significant advancements in other neurological illnesses (e.g., brain tumours, Parkinson's, Alzheimer's, Dementia and Schizophrenia) where previous understandings of structural and functional connectivity could

not fully account for some symptoms and phenomena (Calabresi et al., 2007; Derks et al., 2014; Koshiyama et al., 2021; Lambon Ralph et al., 2007; Sanchez et al., 2012; Vargas et al., 2019) and is central to our progressive understanding of FND in which functional, rather than structural, changes are thought to be a result of deficits in neural activity leading to symptoms (Baek et al., 2017; Kozlowska et al., 2018; Pick et al., 2019). Initially, FND was considered a 'non' or 'feigned' disorder because there was a lack of findings from structural neuroimaging and inconsistent reports through lesion studies and volumetric structure analysis. However, with considerable advancements in neuroimaging techniques and new conceptualisations of the function of the nervous system and brain-body-mind interactions, there has been a significant improvement in understanding this field. Emerging insights are now supporting the reconceptualization of FNDs. Throughout this chapter, a range of neuroimaging studies are reviewed, but importantly evidence from both functional and structural paradigms implicates the role of several neural networks underpinning symptoms in FND (Kozlowska et al., 2018; Perjoc et al., 2023; Puentes, 2023; Voon et al., 2016), including limbic, agency, sensorimotor and attentional circuits (Baizabal-Carvallo et al., 2019; Bègue et al., 2019; Drane et al., 2021; Foroughi et al., 2020; Szaflarski & LaFrance, 2018).

Particular focus has been given to neurocircuitry in limbic/paralimbic circuits owing to symptom profiles in FND, and in such studies, findings suggest increased connectivity between the amygdala and motor control circuits (Aybek et al., 2015; Espay et al., 2018; Hassa et al., 2017; Voon et al., 2010). However, findings involving the amygdala are inconsistent, with reports of hypo, hyper or normal connectivity and differences depending upon FND symptom profile (e.g. functional movement or functional seizure cohorts; Allendorfer et al., 2019; Balachandran et al., 2021). Other implicated areas which present deficits in functional connectivity in FND include the insula, cingulate gyrus, ventromedial prefrontal cortex and right temporal junction (rTPJ) based networks, particularly in self-agency disturbances (Aybek et al., 2015; Cojan et al., 2009; Espay et al., 2018, 2019; Voon et al., 2011; Zito et al., 2020).

Some brain areas implicated in the neurocircuitry of FND are at the intersection of negative affect, nociception, cognitive control, and self- and emotional awareness (Cretton et al., 2020; Deeley, 2016; Edwards et al., 2012), particularly the interaction and interconnection of affect, pain, and cognitive control in the cingulate cortex (Shackman et al., 2011). Some suggest that the neurobiology of FND rests in the implication of neural networks associated with (Milano et al., 2023). Either way, it is clear that neurobiological dimensions add to pathophysiological explanations and explain the brain basis of symptoms in continual

advancements to knowledge in this field (Baizabal-Carvallo et al., 2019; Edwards et al., 2012; Forejtová et al., 2023). Despite discrepancies in findings, these are beginning to be incorporated and developed into research-informed treatments and interventions, particularly CBT and multidisciplinary motor retraining (Espay et al., 2019; Faul et al., 2020).

3.2.3 FND as a disorder of body, brain and mind

The conceptualisation of FND as a neural network disorder represents a significant advancement of knowledge into the disorder, and this chapter will explore these findings further. However, this set of work also encourages further refinement of this idea and consideration of FND as a "whole body" or embodied brain disorder. Whilst research demonstrates the role of neural network dysfunction in FND (e.g. Krujis et al., 2014; Voon et al., 2011) there are also biological markers such as cortisol, heart rate variability and epigenetic changes emerging evidence of bodily biological dysfunctions in FND which could underpin these neuronal network dysfunctions (Asadi-Pooya, 2016; Milano et al., 2023; Villagrán et al., 2021). Mechanisms of psychological importance (e.g., interoception, attention, emotional processing and dissociation) could also contribute toward these states (Elbers et al., 2018; Kozlowska et al., 2015; Ouss & Tordjman, 2014; Szaflarski & LaFrance, 2018) or be a symptom of neural or biological dysfunction.

Contemporary computational models recognise how the embodied brain responds to psychosocial and biological stressors, which can be reconciled with recent neuroscience evidence on the overlapping mechanisms mentioned (Barrett et al., 2022; Muehsam et al., 2017). The brain does not sit in isolation from the rest of the body, and not only does it respond to psychological and biological adversaries, but these mechanisms also interlink and interact. FND goes beyond dysfunctional neuronal networks and is a condition of the embodied brain. Whilst FND patients present with clinical findings suggestive of a disturbance of awareness, we should also recognise that the neural underpinnings of distorted awareness can cause distorted reality and functionality of other bodily mechanisms (Barrett et al., 2022; Milano et al., 2023). This chapter predominantly suggests that FND should be considered as a dysfunction of neuroinflammation wherein chronic inflammation leads to impaired neural networks (and, in chronic cases, impairs neuroplasticity) and results in cognitive and psychological dysfunction.

3. 3. Neuroimaging data and findings

3.3.1 Functional findings

A central idea from neuroscience is that functional networks are organised in the brain along a phylogenetic hierarchy, and this reflects stages of development (Arnsten, 2015; MacLean, 1990). Within such a framework, functional neural networks reflect the dynamic and distinct adaptive challenges, particularly those encountered that influence physiology, cortical arousal and the activation of innate immune defences (Arnsten, 2015; Ding et al., 2013; Hermans et al., 2011). At times of 'attack', functional networks activate innate immune effector cells known as glial cells, particularly microglia and astrocytes, which modulate neuroinflammation and synaptic plasticity (Frank et al., 2016). Research shows that states of calm and safety enhance cognitive and integrative processing skills (Knyazev et al., 2017; Zhang et al., 2012). This type of processing relies on higher-order cognitive functions and is mediated by the prefrontal cortex (PFC), which plays a crucial role in motor planning and control functions, including inhibition and decision-making (Knyazev et al., 2017). As individuals mature, these advanced processes can become functional and activate cortical brain regions. Conversely, exposure to danger or heightened arousal shifts neural processing toward subcortical structures associated with emotion and motor-sensory reactivity and can influence emotion and motor-sensory processing as these become a necessity (Arnsten, 2015).

During these states, catecholamines such as norepinephrine and dopamine are released, impairing the executive functions of the PFC while enhancing reflexive, habitual responses (Hermans et al., 2011). These neurotransmitters influence neural excitability by interacting with glial cells, particularly astrocytes and microglia, which are more abundant in subcortical regions and function as neuromodulates which regulate levels of network excitability and reset basal responsiveness to neural circuits (Ding et al., 2013; Mittelbronn et al., 2001). Astrocytes regulate synaptic transmission and support metabolic homeostasis, whereas microglia contribute to synaptic remodelling and immune responses, modulating neuronal excitability and resetting basal neural responsiveness. Whilst a central focus throughout neuroscience has been on structural findings, functional findings may denote more contemporary views of the neural networks inhibited in FND and provide clues as to the mechanisms underpinning symptoms, particularly in relation to dysregulated motor control and sensorimotor integration.

3.3.2 Structural findings

Structural neuroimaging findings are inconsistent but do implicate that some patients with FND have structural and functional alterations, particularly in areas related to emotion and threat processing, salience, arousal, agency and motor control. Cingulo-insular alterations and structural changes in the salience network are described across FND populations, including functional seizures (e.g. Labate et al., 2012; Vasta et al., 2018) and mixed FND phenotypes (Perez et al., 2018; Radmanesh et al., 2020). The salience network, which includes the cingulo-insular, amygdala and periaqueductal grey is implicated in the processing of interoceptive and nociceptive inputs of affective, threat-related or motivational valence (Seeley et al., 2007). The anterior and dorsal ACC areas are also implicated in executive control, and self and emotional awareness (Sinanaj et al., 2015). Consideration of multimodal integration of these constructs has informed of the integrated nature of these interconnected areas and has informed of likely centres of investigation for FND research to understand sensorimotor, affective and cognitive systems (Bègue et al., 2019) as whole brain paradigms.

Several grey and white matter studies characterise FND as a structural dysfunction (Diez et al., 2021; Kozlowska et al., 2017; Perez et al., 2018; Muarer et al., 2018; Sone et al., 2023), studies in FND samples support the findings of functional studies by implicating similar neural networks, but challenge the notion that FND is purely a result of disrupted neural functioning. White matter investigations implicite possible limbic fibre bundle alternations (Lee et al., 2015; Zhang et al., 2012). This may also depend on prominent symptom subtype for example studies have shown that those with functional seizures may show more lattice-like (small world), white matter organisation and decreased coupling of the strength of functional connectivity profiles with altered structural findings across sensorimotor, attentional, subcortical and default mode works (Ding et al., 2013). This heterogeneity limits conclusions about specific neural signatures but denotes the need for further research of embodied brain paradigms

3.3.3 Task-Based vs Resting-state Findings

Initial neuroimaging studies have focused on motor execution and control circuits in FND, particularly in limb strength between affected and non-affected limbs (Marshall et al., 1997), feigning (Spence et al., 2000), or elements of motor cognition including motor preparation, finger tapping tasks or imagined movements (Burgmer et al., 2006; Cojan et al., 2009; De Lange et al., 2007; Espay et al., 2018; Schrag et al., 2013; van Beilen et al., 2011). More recent studies investigate emotional processing and affective memory (Espay et al., 2018; Sojka et al., 2019), avoidance learning (Morris et al., 2017) and metacognition (Bègue et al., 2018).

To date, only two studies, across two publications, have utilised resting-state fMRI data in adults with mixed FND, though with relatively small sample sizes (*N= 25*; Baek et al., 2017; Morris et al., 2017). Compared to controls, it was found that there was reduced functional connectivity within frontal control regions, anterior cingulate cortex, and the right inferior parietal cortex, along with increased functional connectivity between the premotor cortex and the supplementary motor area and between the amygdala and right dorsolateral prefrontal cortex. The research utilised seed brain regions analysis which limits understanding of connectivity changes throughout the brain however alternative methods, like independent component analysis (ICA) have only been conducted in subgroups of FND like Functional seizures (van der Kruijs et al., 2014) and functional dystonia (Canu et al., 2020) or in child populations (Monsa et al., 2018; Rai et al., 2022). Nevertheless, taken together, the findings are indicative of wide-ranging patterns of alterations in resting state neural networks.

The majority of resting state data in this field has employed Blood Oxygen Level (BOLD) resting-state data from fMRI exploring temporal dynamics in time series data (e.g. Li et al., 2015), rsfMRI in exploring brain networks which analyse the dependency between the time series of different brain regions (e.g. Chen et al., 2020; Foroughi et al., 2020) or seed-based neuroimaging which looks at functional connectivity based upon a seed (region of interest) and the rest of the brain (e.g. Allendorfer et al., 2019; Baek et al., 2017; Szaflarski & LaFrance, 2018; van der Kruijs et al., 2012). Only one study thus far has employed dynamic resting state data which does not rely upon BOLD signals (Marapin et al., 2020), and only a selection has attempted to identify network features with predictive diagnostic potential (Wegrzyk et al., 2018). Whilst a range of innovative methods have been used, these all have limitations (a methodological discussion of which is beyond the scope of this chapter), but importantly, they do not necessarily capture a complete picture of brain architecture and neuronal connectivity.

Evidence from contemporary imaging studies has enabled the identification of functional networks, central to the brain's organisation at rest and in task-evoked states (Raichle, 2015; Williams, 2017). At rest, the default mode network (DMN) is thought to have an important role in self-directed movement, and many other states (Hagmann et al., 2008), and various disorders have been conceptualised more recently as having dysfunctions in this mechanism (Wang et al., 2016; Williams, 2017). DMN also plays a role in energy regulation and supports a wide range of physical and psychological functions, including emotion and pain processing, memory and decision-making (Kleckner et al., 2017). The DMN can be described as a system which is the basis of allostatic-interception decision-making, which allows regulation of the body's physiological systems to regulate energy in times of crisis, as signalled by psychologically and biologically produced states. Chronic or extreme activation of this system increases susceptibility to various disorders (McEwen & Gianaros, 2011). Given findings of HPA dysregulation, ANS and potential neural networks in FND (Apazoglou et al., 2017; Bakvis et al., 2009; Blakemore et al., 2016), it is reasonable to assume that dysfunctions are present in the DMN and this has indeed been found in some subsamples like Functional Seizures and child populations (Kozlowska et al., 2018). Taken together, findings suggest that there could be maladaptive activation of the allostatic-interoceptive brain system (DMN), and this leads to disruption of the motor system and energy levels, also accounting for crash-slump reactions and the adaptable nature of symptoms.

3.3.4 Differences by Symptom Cluster

Differing presentations (e.g., motor, sensory, visual, and Functional Seizures) have been studied using a variety of markers, including neurophysiology, serum biomarkers, cognitive tasks, and functional and anatomical imaging (Voon et al., 2016). Whether symptom presentations have underlying commonalities, i.e., interrelatedness, or differences, remains an important and unanswered question. There are differences in amygdala response with findings in functional seizure cohorts showing hypoactivity or increased connectivity with sensorimotor areas which are not seen in cohorts of functional movement disorder, who show regular connectivity, despite assumptions of similarities in the underlying mechanisms and the findings being more consistent theoretically with the symptoms produced in the latter (Allendorfer et al., 2019; Balachandran et al., 2021; Espay et al., 2018)

In adult patients with functional seizures, fMRI studies have revealed both hyper and hypo connectivity of networks associated with executive control during rested, wakeful states (van der Kruijs et al., 2012), and analysis using seed regions showed enhanced connectivity in areas associated with salience networks amongst others. In later whole-brain analyses, cortical networks as part of the frontoparietal network, executive control and sensory-motor networks showed dysfunction (van der Kruijs et al., 2014). A study with adult patients and movement disorder subtypes showed that areas of dysconnectivity could help differentiate patients from controls (Wegrzyk et al., 2018). Overall, these studies suggest that whilst a common pathology may present in all FND, there may be specific altered connectivity in various networks across FND subtypes or pathophysiologies. Further research is needed to better understand the specific mechanisms underlying these alterations and to develop a more specific understanding of their differences. There needs to be documentation of symptom subtypes within published works.

3.3.5 Neuroimaging Correlates & dissociation correlates

It is possible that dissociation is a negative mediator or prognostic marker in the overall clinical presentation and relates to the severity of FND. Perez et al., (2018) explored cortical thickness using structural MRI and found that higher dissociation (particularly depersonalisation/derealisation) scores correlated with increased right lateral occipital cortical thickness in participants with FND. Van der Kruijs et al., (2012, 2014) utilised fMRI across two studies to explore alterations in connectivity and found significant correlations between connectivity values, mood and dissociation. In a comparison study of those with Functional Seizures compared to healthy controls in resting-state fMRI, those with Functional seizures were found to have increased activation of resting-state networks in frontal-parietal, executive, sensorimotor and DMN networks, and these correlated with all dissociation scores (van der Kruijs et al., 2014). Resting-state data has also revealed default mode network dysfunction and correlates with dissociative states in other conditions including ASD (Starck et al., 2013), borderline personality disorder (Wolf et al., 2011), PSTSD (Schlumpf et al., 2021), Schizophrenia (Wang et al., 2015) and in major depressive disorder (Su et al., 2014; Zhu et al., 2012). However, associations in FND literature remain limited.

Research from neuroimaging has limited its associations with implicated psychological states in FND. However, the broader literature shows that there are factors which should be considered. For example, literature on the neurobiology of loneliness shows that abnormal structure and activity in regions associated with FND typically (Lamb et al., 2021) and that variability in brain structure and

function can occur in response to social support (Schurz et al., 2021), which is often reduced after FND diagnosis. Thus, research should incorporate measures of loneliness and social support into paradigms when exploring FND to ensure that this is not a contraindication to findings. Findings of this nature could not only elucidate the interconnectedness of implicated paradigms in FND under an embodied brain hypothesis. However, they could also promote features of care, for example, social prescribing and increasing social support as part of treatment and recovery to reduce the risk of further illness burden.

Advancing knowledge of the pathophysiology of FND requires informed approaches led by multi-construct exploration, as in biopsychosocial approaches, and with the use of multimodal data, including the incorporation of advancements in neuroimaging (Baizabal-Carvallo et al., 2019; Bègue et al., 2019; Pick et al., 2019; Voon et al., 2016). Motor research has advanced with considerations, for example, of the interplay between motor control and emotion processing in Go/No-Go paradigms (Faul et al., 2020; Hassa et al., 2017) or grip strength in affectively valanced imagery (Blakemore et al., 2016). Prefrontal and paralimbic (orbitofrontal and parahippocampal gyrus) structural alterations have been noted in FND (Kozlowska et al., 2018; Labate et al., 2012; Williams et al., 2018), and these have been linked to dissociation in Functional Seizure subtypes (Labate et al., 2012). Much more research is needed to elucidate neuroimaging findings in relation to social-emotional, metacognition and neurobiological constructs across FND subtypes. However, so far, evidence implicates several psychological correlates for consideration.

3.3.5 Limitations of current Neuroimaging data

In comparison to research on neuroimaging and biopsychological data for other illnesses, FND research remains largely in its nascent stages. The studies conducted thus far have encountered several limitations, including low sample sizes and a lack of replication, resulting in multiple findings discrepancies. Additionally, risk factors vary across patients (Ludwig et al., 2018) and as outlined in Chapter 1 of this thesis and this lends to the consideration of individual differences, differences in developmental trajectories, and gene-environment interactions amongst other variabilities in underlying mechanistic states and neural network function (Apazoglou et al., 2018; Diez et al., 2021; Ferrarese et al., 2022; Keynejad et al., 2019). Patients with FND also have high rates of comorbidity, including other physical states (pain, fatigue) or mood disorders (e.g. anxiety, depression) or have high rates of dissociation (as outlined and reviewed in Chapter 2; Goldstein et al., 2020; Kranick et al., 2011; Nicholson et al., 2020). There is significant variability in the presentation of these

additional commodities. Emerging evidence of high comorbidity with ADHD/ASD in FND (Asadi-Pooya et al., 2023) where heightened and altered connectivity of neural networks has long been established, has also been recently found and needs to be considered in FND research.

There are several considerations which need to be made when conducting research, particularly neuroimaging or neurobiological research on an FND sample. Those with FND can present with varying symptom presentations, and these can change and fluctuate throughout the illness (McKenzie et al., 2011; Nicholson et al., 2020) and some experience turbulent and chaotic illness narratives which are akin to slump-crash reactions seen in other chronic conditions. Duration and onset should be considered as neuroimaging correlates could vary (including additional compensatory changes over time; Newbold et al., 2020). Other considerations must be made to avoid heterogeneity, including symptom severity, sample characteristics (as neural connectivity changes across the lifespan and paediatric samples cannot be easily applied to adult samples), persistence and regularity of symptoms and symptom location. Currently, the limited scope has left researchers to interpret data across FND subtypes, and whilst there are many overlapping symptoms and likely a core underlying mechanism, there are differences to consider (Gelauff & Stone, 2016). For example, whilst those with functional tremors may also show functional weakness or deficits in the same limb or have additional functional seizures (Gelauff et al., 2020; Martin et al., 2017), there also needs to be consideration given to differences in patterns of neural network dysfunction (Allendorfer et al., 2019; Balachandran et al., 2021).

In addition to the usual constraints and limitations of the above neuroimaging methodologies and of task-base and block design studies, neuroimaging research to date has failed to consider other theoretical constructs of theoretical relevance to the pathophysiology of FND (Drane et al., 2021; Edwards et al., 2012; Koreki et al., 2020). fMRI is viewed as a pinnacle of neuroimaging technology, but an overreliance on a single methodological exploration limits the focus and scope of research endeavours and negates the need to explore other FND markers and holistic, multimodal approaches. These would enhance the development of newer theoretical constructs which are essential to the progression of understanding of the pathophysiology of FND.

3.4. EEG

3.4.1 Applications of EEG

Despite its inception in 1924 (by Hans Berger), electroencephalography (EEG) has not received commensurate attention in FND research. This disparity may be attributed to the delayed emergence of neuroimaging technologies in FND research, coupled with prevailing preferences for fMRI and BOLD contrast and newer neuroimaging technologies. However, it is imperative to acknowledge the inherent limitations of newer methodologies. EEG can offer insights into dynamic brain activity, with good temporal resolution and, importantly, information on electrical activity using non-invasive, millisecond-precision data. This can complement data from hemodynamic measures derived from BOLD technologies. EEG has been used as a tool to differentiate Functional Seizures from epilepsy, as there are differences in the electrical profile of these (Popkirov et al., 2017). The EEG Bereitschaftspotential can also be used to diagnose Functional Movement Disorder subtypes (Thomsen et al., 2020), though it is not commonly used in clinical practice. However, this limited use of EEG underpins typical stereotypes of FND as an exclusionary diagnosis (E.g. Herbert et al., 2021), and EEG can be utilised beyond this as a cost-effective solution providing positive diagnostic markers and innovative solutions to explore brain activity and neural networks.

EEG signals reflect amplified extracellular activity surrounding postsynaptic neurons, which can be recorded at the scalp (Berger, 1929). It is, therefore, a relatively direct measure of underlying electrocortical activity through measures of extracellular potentials, predominately from pyramidal cells (Purpura & McMurtry, 1965). Electrocortical signals are generated by the synchronous firings of thousands of excitatory and inhibitory postsynaptic potentials (Cohen, 2014, 2015). For EEG and MEG sensors to detect these signals, around 10,000-50,000 pyramidal cells need to be firing simultaneously (Murakami & Okada, 2006). This is possible because the pyramidal neurons are aligned in parallel and have cell bodies large enough to create a detectable electric field.

There is an underutilised potential for quantitative EEG (Fonseca et al., 2015), which can be used to estimate the frequency of brain oscillations denoted by power values and calculate connectivity indices. Recent studies demonstrate that brain oscillations reflect mechanisms of cerebral integration across several functional domains (Arikan et al., 2021; Frauscher et al., 2015) measured using EEG. Various frequency bands (such as alpha, beta, gamma, delta and theta) can be explored to provide valuable insight into distinct cognitive processes and brain

states to understand neural mechanisms and identify abnormalities or patterns of activity. Briefly, higher-frequency bands in EEG (alpha, beta, gamma) are associated with processes associated with higher-order cognitive function, including those of theoretical importance to FND (Knyazev, 2017). For example, alpha oscillations have been implicated in attentional processes, while beta oscillations are associated with motor control and executive functions (Putman et al., 2014; Schmidt et al., 2019). Gamma oscillations are often observed during cognitive integration tasks but there remains much debate over their functions (Buzsáki & Wang, 2012; Herrmann & Demiralp, 2005). Lower frequency bands (delta, theta) are associated with more primitive mechanisms, including attention, drowsiness, memory, movement, learning, emotion regulation and spatial navigation, as well as the maintenance of bodily functions (Buzsáki & da Silva, 2012; Frauscher et al., 2015). Exploration of frequency bands in EEG is essential for understanding neural dynamics and the neurobiological mechanisms which underpin the disorder.

In addition to brand frequency exploration, which can be obtained from resting state data, task-based data can utilise event-related potentials (ERPs), and electroencephalographic signals, which are time-locked to the presentation of behaviour or stimulus. ERPs can be interpreted as a product of the subcomponents which reflect the processing of stimuli (Luck, 2014, 2016). ERPs can be employed to investigate cognitive processes by examining the amplitude and timing of positive and negative deflections following experimental manipulations. These manipulations may alter subsequent components, consequently influencing amplitude and latency. Whilst studies often use a few select channels for statistical frequency and to minimise interference of artefacts, additional methods of analyses like independent components analysis (ICA; Stone, 2004) can help to ensure that neuronal source inferences are not lost. ERPs can, therefore, serve as a valuable tool to comprehend neurophysiological abnormalities associated with neurological disorders.

EEG methods are not without their limitations. For example, both ERP and frequency data may be relatively small and thus difficult to discriminate from signal trials (Luck, 2006). As such, compensatory considerations must be made, including the averaging of ERPs across multiple events and considerations of the duration of baseline recordings for frequency data. Both methods have the ability to remove unwanted modulations in the data and enable the general averaged waveforms. Additionally, these methods may offer an advantage over hemodynamic measures (e.g., fMRI and PET) in explorations of functional activity because of their increased temporal resolution (milliseconds instead of several seconds; Luck, 2005; Otten

& Rugg, 2005). Additionally, advancements in analytical techniques for EEG, including machine learning and neural network analysis, have advanced other long-established areas of investigation like epilepsy (Acharya et al., 2018; Caruana & Niculescu-Mizil, 2006; Kasabov, 2019) and further advanced knowledge of FND by providing valuable insights into the underlying mechanisms.

3.4.2 EEG Findings in FND

EEG studies in FND have included assessment of spectral power, source localisation and event-related potentials (Barzegaran et al., 2016; Hallett, 2006; Kozlowska et al., 2018; Meppelink et al., 2016; van der Salm et al., 2012). Quantitative EEG can be used to estimate the frequency of brain oscillations and calculate indices of neural connectivity in clinical populations (Alper et al., 2006; Boord et al., 2007; Nagata et al., 1989). Studies using EEG in children and adolescents with FND have found increased automatic and cortical arousal and increased activation of nodes of the Default Mode Network (DMN), salience network (dorsal ACC/dorsomedial PFC), and supplementary motor area (SMA) in resting state studies (Kozlowska et al., 2018; Radmanesh et al., 2020).

Resting-state quantitative EEG has explored Functional Seizure subtypes and has found areas of interest across frequency bands, including decreased gamma synchronisation between frontal and posterior regions (Xue et al., 2013) and decreased functional connectivity in widespread critical regions in the alpha band (Barzegaran et al., 2016) and heightened gamma-band spectral power in left parietal region with lower gamma band spectral power in the right temporal region (Umesh et al., 2017). A recent study found that both beta and gamma oscillations were higher in those with functional seizures than in an epilepsy control group (Rai et al., 2022). Whilst these findings apply to those with Functional seizures and more data is needed across subtypes, and the findings may not yet provide useful tools as a positive diagnostic marker, these quantitative EEG alterations are indicative of the underpinning neural mechanisms of FND and suggest high-frequency oscillations in central motor and somatosensory cortices may be of particular relevance. EEG markers of functional axial jerks have also been proposed: event-related desynchronisation (ERD) in the broad beta band (Meppelink et al., 2016). Reductions of beta and low gamma oscillations occur prior to cued and self-paced movement (Pfurtscheller & Aranibar, 1977) and may reflect changes in self-

directed attention, as recently highlighted in current models of FND (Edwards et al., 2012). However, further enquiry is needed to understand its role and the role of EEG more generally in ascertaining pathophysiology across subtypes and in relation to the production of diagnostic markers.

In relation to multi-state analysis of EEG in FND, a child and adolescent sample of those with mixed symptoms (though 51% functional seizure subtype), found increased theta and delta in electrode clusters corresponding to the DMN and a trend toward increased theta and delta oscillations in the salience network (Kozlowska et al., 2018). In a presumed reaction time task, patients with Functional weakness showed larger P3 event-related potentials (ERPs) when symptomatic hands were pressed as well as smaller, earlier N1 potentials in comparison to weighing subjects. Abnormal N1 processes could reflect abnormal processing of pre-cues and the enhancement of P3 could be related to the suppression of brain circuits involved in the attribution of agency (Blakemore et al., 2016). Currently, the definition of BP is a clear and slow negative electrical shift which occurs over the central cortical areas and increases over time at 1 – 2 seconds before movement onset (Zutt et al., 2017). However, a quantitative resting-state EEG would be highly desirable to standardise diagnosis. There is the suggestion that combining the BP with the assessment of event-related beta desynchronisation increases sensitivity (Meppelink et al., 2016). This emphasises the importance and necessity of improving electrophysiological biomarkers of FND.

3.4.3 EEG and Dissociation

As dissociation is frequently reported in FND (as reviewed in Chapter 2), consideration needs to be given to its association with neural network findings. To date, only two studies have employed EEG to explore connectivity in patients with FND and its relationship to dissociation. (Xue et al., 2013), in a small sample (N = 15 participants with Functional Seizures and 15 healthy matched controls) found that the Functional seizure group had less connectivity between frontal and posterior brain regions relative to controls but found no correlations with the Somatoform Dissociation Questionnaire (SDQ) used to measure dissociation scores. Conversely, using the same measure of dissociation, Kienle et al. (2018) studied a mixed FND sample and found associations between cortical indices of emotion regulation correlated with SDQ dissociation scores. As previously identified, the application of contemporary notions of

dissociation needs to be employed in multimodal analyses of a wide range of neurobiological data methods, and consideration should also be given to correlates of other potentially conflicting or underlying psychological correlations in FND.

3.5 Neurochemical

Whilst neuroimaging and EEG studies in FND are widely cited as being in their infancy, neurochemical and molecular research in FND fields is even more nascent. There are likely several contributing factors to this including funding constraints, lack of awareness in molecular biology fields of application and suitability, institutional priorities, academic silos and limited opportunities for cross-disciplinary collaborations. However, increasingly, researchers are turning to the exploration of biomarkers across domains which could improve upon gaps in the current knowledge of systems-level interactions of FND and contextualisation of automatic, endocrine and inflammation understandings to understand the neural correlates of FND. Such efforts would not only support research but could lend toward the advancement of further biologically informed positive diagnostic markers and treatment options.

3.5.1 Neurochemical Findings in FND

As stress has long been considered to be a psychological and (more recently) a biological predisposing risk factor for the development of FND (as outlined throughout chapters 1 and 2), neurochemical investigations have utilised this as a theoretical starting point for exploration of potentially related biomarkers. For example, cortisol (a steroid hormone) is implicated in many bodily functions and states (Erickson et al., 2003), but is most commonly known for its association with stress and health (Young et al., 2004). Cortisol is a major glucocorticoid which has many diverse functions, including adaptive plasticity in the brain (in conjunction with amino acids), circadian rhythm and can be an indicator of allostatic load and stress (Katsu & Baker, 2021; Lightman et al., 2020; McEwen, 2019; Sherman & Mehta, 2020).

Current cortisol studies in FND show very mixed results and methods are variable (Apazoglou et al., 2017; Bakvis et al., 2009; Chung et al., 2023; Maurer et al., 2015; Novakova et al., 2017; Weber et al., 2024; Zhang & Liu, 2008). Overall, there seems to be a consensus that there are similar baseline levels as controls and this was further implied by a recent meta-analysis (Paredes-Echeverri et al., 2022). Task-related cortisol responses show that salivary

cortisol correlates with some psychological and cognitive correlates and may distinguish between some subtypes of FND (Apazoglou et al., 2017; Bakvis et al., 2009; Chung et al., 2023; Weber et al., 2024). Whilst research on cortisol may indicate dysfunction in HPA regulation in some studies, there are dynamics between this molecular compound, HPA axis function and other neurochemical and physiological circuits and these findings have not been consistent. This could be a result of many factors which influence cortisol secretion (Lightman et al., 2020). Owing to the variability of this cytokine and its lack of specificity (Chrousos, 1995), other recognised inflammatory markers like Interlukin-6 (IL-6) and C-reactive protein (CRP) may be more reliable as markers of systemic inflammation (Gabay & Kushner, 1999; McInnes & Schett, 2017; Povoa et al., 2005; Ridker et al., 2000). Much more work is needed in this area of research to understand the heterogeneity and to express cortisol levels and other differences in relation to other catabolites in establishing the neurochemical markers of FND and establishing the role of inflammation.

Oxidative stress levels and s100B (a calcium-binding protein which is indicative of brain injury and neurogenerative disease) levels in children with FND were not significantly different from those in healthy controls (Sizer et al., 2023). Compared with healthy controls, those with functional seizures show increased urinary epinephrine excretion in the morning and decreased excretion in the afternoon, suggestive of time-dependent changes (Aydin et al., 2011; Ceylan et al., 2018). These findings could provide support of neural network dysfunctions in the CNS and could be used as biomarkers to distinguish Functional Seizures from other seizure forms. Other studies have investigated differences in FND in neuropeptide Y, norepinephrine, ghrelin, testosterone, progesterone and oxytocin, but there is little empirical evidence to formulate concrete arguments in these areas (Aydin et al., 2011; Ceylan et al., 2018; Miani et al., 2019; Winterdahl et al., 2017). Further potential biological markers should be explored to understand the aetiology and diagnosis of FND.

There is a lack of studies and evidence concerning the potential role of genetic predispositions. However, a small case study did report that a positive family history can be seen in those with functional movement disorders (Batla et al., 2013). The genetic vulnerability may predispose some to react to environmental factors and lead to the onset of symptoms. For example, a preliminary study identified that methylation rates of oxytocin receptor genes (studies of which help to elucidate the mechanisms under which gene expression is induced) are increased in those with mixed FND types (Apazoglou et al., 2018). Such promising studies

need to be followed up and may illuminate the role of gene-environment interactions in the aetiology of FND as much as biopsychosocial interaction consideration is needed.

3.5.2 Inflammation

The immune system and brain constantly engage in bidirectional communication through several neural and hormonal pathways. The inflammatory response is a universal adaptive mechanism triggered by physical injury, metabolic stress, trauma, and disrupted homeostasis. Neuroinflammation is mediated through the production of cytokine (Becher et al., 2017; Dantzer et al., 2008), including commonly studied proinflammatory cytokines such as interleukins (e.g. IL-1β, IL-2, IL-6) and TNFα. High concentrations of pro-inflammatory cytokines in response to infection are adaptive responses which contribute to survival during infection (Dantzer et al., 2008). The known symptoms of high concentrations could cause any of the so-called "somatoform" symptoms seen in FND, including drowsiness, fatigue, cognitive fog or 'fugue', joint pain and reduced social activity.

However, states of neuroinflammation and chronic inflammation have begun to be identified in FND; for example, van der Feltz-Cornelis et al. (2021) assessed cytokines in FND and found elevated levels of IL-6 & TNFa in a relatively small cohort (n=14). Fluctuations in the concentration of cytokines (particularly anti-inflammatory cytokines) in the brain are known to affect other physiological processing, including the formation and organisation of neural networks, and, as a result, influence cognitive functions (Dantzer & Kelley, 2007; Levin et al., 2021). Additionally, fluctuations in the concentration of cytokines can affect many physiological processes and could explain slump-crash reactions in FND symptomology. In addition to their role in the immune system, cytokines (small-molecule signalling soluble proteins) play an essential role in the development and maintenance of physiological and pathological processes, providing co-ordinated interaction of cells throughout the body and brain and affecting many functions including thermoregulation, eating, sleep, emotion, cognition, learning and memory amongst other cognitive functions through their roles in the modulation of synaptic neurotransmission, neuroplasticity and cognitive function (Becher et al., 2017; Levin & Godukhin, 2017; McAfoose & Baune, 2009; McKim et al., 2016; Osipova et al., 2018).

Whilst the pathogenesis and specific origins of FND are unknown, a proposed underpinning mechanism is systemic low-grade inflammation (Kovacs et al., 2016; Tiyekli et al., 2013; Vogelzangs et al., 2013). Elevated CRP has been identified in children with FND (Kozlowska et al., 2019) and may indicate adverse life experiences, but it has also been implicated in motor function (Tak et al., 2009) and may be an inflammatory process (Ratcliff & van der Feltz-Cornelis, 2020). For example, autonomous dysregulation could interfere with the downregulation of corticosteroid production in the adrenal glands and result in peripheral inflammation, which cannot easily be reversed (Pongratz & Straub, 2014). Whilst previous studies have inferred that such findings are a result of trauma (Baumeister et al., 2016), they could also be a result of biological trauma. For example, they could result from the dysregulation of stress states as a result of chronic inflammation or a biological assault, as opposed to simple psychological ALEs. This could underpin how neuroinflammation affects brain activity, accounting for the findings of disruption to information processing (de Vroege et al., 2021; Baumeister et al., 2016). Again, it is important to acknowledge that different typologies of FND symptoms could show varying levels of molecular dysfunction, whilst different levels of neuroinflammation could also explain the differences in symptom presentation (Ratcliff & van der Fleltz-Cornelis, 2020). Initial data suggests that there are notable differences across inflammatory markers in FND, but much more research is needed in this area to define underlying mechanisms (see Paredes-Echeverri et al., 2022 for review).

3.5.3 Inflammation and Dissociation

When investigating psychological correlates of inflammation, it is also important to consider the principles of allostasis, a term coined by Sterling (1988) in which the ANS and HPA axis promote adaption to multiple states. However, they can cause problems for the brain and body if homeostasis is not maintained or if a stressor (be that a biological, social, environmental or psychological trauma) causes systems to be over or under-active. This dysfunctional or erratic state can lead to detrimental effects of allostatic load (McEwen, 2003), which subsequently has an impact on other systems, which in turn fail or overreact. Indeed, many of the risk factors for allostatic load map onto the epidemiological profile of and known risk factors for FND (see Suvarna et al., 2020 for review) and are known to have health implications across a range of health conditions (Brody et al., 2013; Duru et al., 2012; Guidi et al., 2020; Von Korff et al., 2009). Dissociation, too, has been implicated in this relationship as

a potential psychobiological reaction to allostatic load (Grassi-Oliveira et al., 2008; Lamb et al., 2021; Staniloiu et al., 2010).

Whilst the relationship between FND and other disorders, such as Myalgia Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS), remains controversial, several studies have investigated biomarkers in other "medically unexplained diagnoses". These studies have produced conflicting evidence regarding acute and chronic stress responses, as well as autonomic, endocrine and inflammatory biomarkers. However, the findings suggest a role for allostatic load – the cumulative physiological burden of chronic stress. Many of these studies were limited by small sample sizes, a narrow focus on singular symptoms, and a lack of comprehensive assessment of broader systemic dysfunction (Nater et al., 2011). The allostatic load was recently measured by an index of 11 biomarkers of metabolic, cardiovascular, inflammatory and HPA and ANS activity and particularly implicated high levels of IL-6, CRP and lower cortisol, which could support this model of inquiry in FND (Keynejad et al., 2019). Clinical heterogeneity through this model likely reflects multiple potential aetiologies and perhaps levels of dissociative tendencies, which, whilst not measured, can be inferred from previous findings. There are also wide-ranging environmental influences which significantly influence biomarkers, and thus, larger samples coupled with neuroimaging data are needed to establish further relevance of the findings.

Metacognitive and psychological processes commonly reported in FND (de Vroege et al., 2021) could be indicative of neuroinflammation affecting brain activity and, thus, neurocognitive function, and these are important to consider in models and in treatment outcomes (de Vroege et al., 2021). Exposure to ALEs in childhood is known to predict DNA methylation patterns, which are known to be a risk for the development of other disorders (Dunn et al., 2019), further demonstrated in gene-environment interaction and epigenetic studies (Lin et al., 2020). Biological, environmental, social and other risk factors associated as being predisposing and precipitating risk factors in FND are also known to be risk factors for neuroinflammation and propensity to development of chronic inflammatory states and/or leading to dysfunction of neural connectivity in other conditions (Bachmann et al., 2020; Huang et al., 2019; Oldenburg et al., 2020; Stevenson et al., 2020)

In exploring the psychological correlates of FND, a study exploring the cortisol awakening response using salivatory cortisol showed that dysregulation of this in FND correlated with ALEs (particularly childhood adverse experiences) and subjective distress

(Chung et al., 2023). The findings, however, did also support that neural underpinnings of FND may extend across arousal-processing and emotional-processing systems. When coupled with previously discussed literature, findings may also infer that with further research, degrees of dysregulation of some neural findings may also correlate with cognitive processing and motor-sensory dysfunction in FND. Dissociation is known as a symptom in many other conditions and has been correlated with systemic or chronic inflammation in IBS (Ferrarese et al., 2022), PTSD and MDD (Powers et al., 2019) and as an outcome measure for those with autoimmune diseases wherein childhood trauma and alexithymia are also known risk factors (Macarenco et al., 2021). Systemic and chronic inflammation is also known to occur more commonly in women (though rationales for this vary it likely contributes to known autoimmune disease) and at specific developmental ages which could account for the epidemiological profile of FND patients (Beydoun et al., 2020; Kushnir et al., 2016; Lawn et al., 2022; Perruccio et al., 2017). However, these associations have not been well studied in FND.

3.5.4 Inflammation and Neuroimaging

Neuroimaging research has postulated dysregulation of the HPA axis in patients with FND, but its relationship to anatomical and biological states remains to be elucidated. Weber et al. (2024) study explored the HPA axis in relation by utilising cortisol awakening response and diurnal baseline cortisol in 86 patients with mixed symptom profiles. HPA dysregulation and changes in glucocorticoid signalling on a molecular level may contribute to increased vulnerability to FND because of epigenetically mediated changes to the neural networks implicated (Chung et al., 2023). However, these changes could also result from the biological insult posed by FND, and changes could reflect effect rather than causality. Cortisol is a cytokine and one of the low basal level indicators of inflammation along with IL-1 and TNF-alpha which influences neuroplasticity and results in impaired cognitive functions, decreased attention and motivation, deterioration of memory and learning, decreases in orienting reaction among other neural networks and cognitive functions (DiSabato et al., 2016; Levin et al., 2021). However, cortisol levels can be influenced by various factors beyond inflammation (e.g., such as stress, medications and circadian rhythm) and its lack of specificity coupled with diurnal fluctuations may limit its reliability as a sole biomarker for inflammation (Chrousos, 1995). IL-1 and TNF-alpha are important measures, yet these indicate more localised rather than systemic responses and relatively short half-lives in circulation, all influencing their stability

as biomarkers of inflammation (Dinarello, 1996). Inflammatory markers like IL-6 and CRP are recognised as key markers of inflammation, and studies have established their roles as reliable markers of systemic inflammation (Gabay & Kushner, 1999; McInnes & Schett, 2017; Ridker et al., 2000; Povoa et al., 2005). Theoretical links are implied of the role of inflammation in FND but studies have yet to explore reliable and stable trait markers. Further, studies in FND have yet to integrate molecular and neuroimaging for holistic understandings; combinations of neuro-molecular components should be explored in the same study for a holistic image of cytokine modulation in FND.

3.6 Chapter conclusion

Chapter 3 has outlined the current understanding of neural networks, structural imaging and EEG in FND. Whilst findings of implicated networks are beginning to be understood there are a wide range of limitations which prevent research from being able to draw clear conclusions from the data thus far. Currently, EEG is underutilised as a research tool in explorations of FND, despite its utility, and the chapter indicates that EEG and electrophysiological data, coupled with newer methods of analysis, such as neural network analyses, may be helpful in furthering understanding of FND. Neuroimaging data has often failed to have large sample sizes and robust symptom classifications and has failed to correlate findings to psychological and cognitive constructs in FND. Thus, there are calls for multifaceted studies which combine various constructs to elucidate better the complex interplay of mechanisms in FND, which this thesis aims to address.

In addition, this chapter has described the current neurobiological understanding of FND, beyond neural network hypotheses. Emerging findings particularly implicate the potential theoretical role of inflammation as a mechanism of interest in FND. While this research is only beginning to emerge, there is a clear need for further explorations in this area, particularly in the combination of psychological and cognitive correlates with both inflammatory and neuroimaging analyses.

Chapter 4: Thesis Aims

4.1 Introduction

The preceding chapters have evaluated the emerging conceptualisations of FND which have expanded beyond initial conceptualisations on which classification systems are based. Contemporary conceptualisations employ neuroscientific evidence to consider FND as a disorder of neural network dysfunction, and emerging insights of FND are considering the disorder beyond this as a disorder of the embodied brain. Several key areas of investigation have been proposed that would have implications for advancing diagnosis, treatment and care provisions. Firstly, a study of dissociation, among other psychological constructs, should be empirically investigated from a biological perspective. Second, there is a need to address the heterogeneity of FND by statistically delineating subtypes based on symptoms, triggers and underpinning biological mechanisms. This may help resolve some inconsistent findings regarding implicated neural networks, particularly in mixed types. Thirdly, as a relatively inexpensive, reliable, non-invasive and direct measure of brain electrical activity EEG should be more extensively used to understand brain function in FND, with the view to identifying positive diagnostic markers. Finally, the role of the immune system, particularly the presence of raised inflammation, should be investigated as underpinning alterations in brain function and associated symptoms in FND.

Owing to a lack of multimodal data in this field, this thesis also aims to converge findings to provide a holistic view of FND, a new model of which is proposed based on findings in the discussion, Chapter 8. An overarching objective of the current thesis, therefore, is to study the relationships across measures of inflammation, dissociation, and brain function in FND. To this end, a series of experiments is proposed involving mixed subtypes of FND in adults aged over 18 years. Novel assessment and analysis methods will be employed with the aim of delineating subtypes of FND and discovering novel positive biomarkers.

The first experiment (Chapter 5) builds upon my undergraduate and postgraduate studies of FND and investigates the role of dissociation in FND and other chronic illness-induced psychological facets. The results from this study inform whether dissociation should be considered in the model of FND, which builds throughout this thesis. Chapter 5 aims to address the following research questions: 1) Is dissociation higher in FND than in healthy

controls? 2) Do dissociation scores differ in FND compared to other long-term conditions? 3) Does social isolation or social support influence dissociation scores in FND? 4) Are cognitive flexibility, resilience and hopefulness related to dissociation scores in FND?

Chapter 6 presents a second cross-sectional study that empirically investigates subtypes of FND. It uses a novel statistical method (for the field), Latent Class Analysis (LCA), to answer the following questions: 1) Do subtypes exist in FND which can be characterised by clusters of symptoms? 2) Do these symptom clusters hold a relationship with the precipitating factor in FND? 3) How is dissociation differentially associated with FND subtypes? 4) Are there other characteristics of clusters or subtypes of symptoms in FND?

Chapter 7 investigates pro-inflammatory molecules in FND, as compared to people without FND and in relation to symptoms and brain function (EEG, resting state data). This multimodal exploratory study aims to address the following questions: 1) Are there differences in inflammatory markers (IL-6 and CRP) in FND compared to healthy, matched controls? 2) Are these differences maintained when mediations are considered for anxiety, depression, stress, BMI and dietary inflammation? 3) Do inflammatory markers correlate with dissociation and are these different in FND compared to healthy controls? 4) Do baseline EEG measures correlate with inflammatory markers in FND? 5) Do dissociation scores and baseline DMN data significantly differ in FND compared to healthy controls?

4.2 Summary of Thesis Aims

1) To explore the role of dissociation in FND and its relationship to other psychological correlates of chronic illness (stress, anxiety, depression, resilience, social isolation and social support)
2) To statistically explore the presence of potential subtypes of FND through LCA analysis of clusters; and their relationship to dissociation types
3) To determine the role of the DMN and neural activity in FND; and the role of dissociation in this relationship
4) To determine if there is a role of inflammation in FND by exploration of biomarkers. Additionally, to explore if this relationship maintains when mediated by dietary inflammation, BMI, age, sex, anxiety, depression and stress.
5) To explore the potential correlates between baseline EEG measures
6) And to measure DMN in relation to biological markers of inflammation and dissociation.

Chapter 5:
Dissociation and its relationship to other neuropsychological correlates in FND

5.1 Chapter Overview

The previous chapters have reviewed the psychological, neurobiological, neuroimaging and electrophysiological constructs in the formulation of a series of research questions sought to advance multifaceted perspectives of the underlying mechanisms and pathophysiology of FND. The current chapter presents the first of the empirical studies conducted as part of this thesis, exploring the relationship between dissociation and other psychological constructs in FND.

A portion of the data presented in this chapter was included in a recent publication (Blanco et al., 2023) as part of a multi0study paper. That publication incorporated the findings from three distinct studies: Study 1 (undergraduate research), Study 2 (master's research), and Study 3 (which included some data from this chapter). However, the current study within this thesis is independent of the publication and expands upon the prior work through unique analyses, a broader range of measures, and a distinct research focus. Specifically, while Studies 1 and 2 in the publication found no association between adverse life events (ALEs) or mood and elevated dissociation scores in FND, this study builds on those findings by employing an alternative dissociation scale, analysing a larger sample size, and incorporating additional variables such as cognitive flexibility, social support and resilience. Furthermore, the data for this study was collected during the pandemic, providing a unique opportunity to examine the effects of social isolation across three groups: individuals with FND, individuals with other long-term conditions, and healthy controls. By situating this study within the broader research context whilst maintaining its distinct contributions, this chapter aims to further elucidate the relationship between dissociation and psychological factors in FND.

5.2 Introduction

As outlined in the previous chapters, FND is broadly defined as motor, sensory, and cognitive dysfunction occurring in the absence of identifiable organic disorder or other

neurological disease (APA, 2013). It is associated with significant impairment in quality of life, psychological functioning and social participating, leading to substantial healthcare costs (Carson et al., 2011). While various biopsychosocial models have been proposed to explain its development and maintenance, no single framework fully accounts for the heterogeneity of symptoms. One factor increasingly implicated in FND is dissociation, which has been linked to disruptions in sensory-motor integration and atypical emotional processing (Kozlowska, 2017) and could account for findings of atypical sensory processing (Brown et al., 2007; Pick et al., 2017) and altered processing of sensory-motor signals (Edwards et al., 2012; Van den Bergh et al., 2017) in FND. Some subtypes of FND also show atypical emotional function (Pick et al., 2019) or prominent alexithymia (the inability to identify one's own feelings; Demartini et al., 2016; Steffen et al., 2015), and it is often considered that FND has a co-occurrence with mood disorders (Brown & Reuber, 2016; Pick et al.., 2016). However, little is understood about the potential underlying mechanisms for FND, nor the relationships between them, and current models fail to account for all symptoms and varying degrees of severity; continued research in this field is essential for advancing knowledge of the condition.

Dissociation has long been considered as underpinning FND (since the work of Janet, 1907) and remains upheld by the World Health Organization's (WHO, 2018) classification, which defines FND as a "dissociative neurological symptom disorder". On the other hand, DSM-5 has adopted "functional neurological symptom disorder", categorised as somatic symptom disorder. As mentioned in Chapter 2, dissociation refers to a pathological process of disconnection in which sensory awareness is altered or there is a loss of typical integration of mental processes, including sensorimotor functions, emotions, memories, awareness, movement, thoughts and affect (WHO, 1992). Subtypes of dissociation may include *detachment*, an altered state of consciousness in which there is separation from the self (*Depersonalisation*), or the world (*Derealisation*) and *compartmentalising*, an inability to deliberately control actions or cognitive processes that would normally be amenable to such control (Holmes et al. et al., 2005). Expansion of the concept of dissociation has not been without controversy either, though recently, there has been a shift away from unitary models, which we critiqued for obscuring nuances between types of dissociation in favour of recognition of dissociative types and multifactorial measurements for dissociation (Briere et al., 2005, 2016; Holder, 2013). Biopsychosocial frameworks acknowledge dissociation as a predisposing factor for FND (McKee et al., 2018) rather than a symptom or precipitating factor, which the study aims to explore from a multifactorial rather than unitary model perspective.

The role of dissociation in FND is in part supported by the co-occurrence of FND with other dissociative disorders (e.g., dissociative identity, dissociative amnesia), which may reflect shared risk factors (e.g., traumatic life events, hypnotic susceptibility) and/or biological mechanisms (Brown et al., 2007). Moreover, in self-report scales, individuals with FND show higher psychological (Goldstein & Mellers, 2006; Perez et al., 2018; Reuber et al., 2003; Şar et al., 2004;) and somatoform (Brown et al., 2013; Pick et al., 2017; Sar et al., 2009) dissociation, particularly in Functional Seizure (previously Non Epileptic Attack Disorder; NEAD) subtypes (Prueter et al., 2002) to a similar degree as in borderline personality disorder and post-traumatic stress disorder (PTSD; see meta-analysis by Lyssenko et al., 2018). Further evidence for dissociation in FND comes from findings that normal muscle power or changes in the frequency or character of tremors are observed when an individual with FND is distracted from the movement (Carson et al., 2015; Daum et al., 2015). Hoover's tests are commonly used as positive diagnostic tools with high specificity for FND (McWhirter et al., 2011), suggesting issues with distorted attention across the patient group. Recently, studies have found that reduced interoceptive awareness is associated with increased dissociation in Functional Seizures (Yogarajah et al., 2019) and FND (Pick et al., 2020), which could account for clinical observations of sensory disturbances and loss of sense of internal bodily changes. Thus, dissociation appears to be a common feature across FNDs, though research has yet to establish this or the potential causes of heightened dissociation in FND (for example, if this is a symptom of the illness or a result of other mechanisms such as mood, trauma or loneliness) and this has yet to be considered explicitly in theoretical models.

To better understand dissociation in FND, it is necessary to explore potential correlates that may influence dissociative experiences and symptomology. While dissociation historically has been linked to adverse life events and trauma (Diez et al., 2020; Levita et al., 2020; Myers et al., 2019; Wieder & Terhune, 2019; Williams et al., 2020), recent evidence (as previously discussed) suggests that FND is not always trauma-related. Rather, trauma appears to be a risk factor for a small subset of individuals with FND, highlighting the need to examine additional mechanisms underlying dissociation in this population (Nicholson et al., 2020). In addition, many would argue that experiences of becoming ill post diagnosis and the subsequent impact on quality of life as a result of symptoms or other biopsychosocial experiences could lend to a raise in dissociative experiences. Given the heterogeneity of dissociative experiences in FND, it is crucial to consider a broad range of cognitive, affective and social processes that may contribute to dissociative symptoms or buffer against them. Expanding this evidence base is

also necessary to positively differentiate FND from other disorders and refine theoretical models of symptom development.

In Edwards et al., (2012)'s prevailing model, FND is framed as arising from distortions between top-down and bottom-up processing, implicating (though not directly suggesting) dissociation in the separation of (normally integrated) executive control functions. This conceptualisation aligns with mechanisms proposed in other conditions characterised by executive dysfunction, such as ADHD (Mattfeld et al., 2016) and certain positive symptoms in schizophrenia (Akbey et al., 2019; Sumich et al., 2018, 2008). While these conditions, like FND, lack definitive biomarkers and remain subject to diagnostic debates (much like FND), they do provide valuable frameworks for understanding dissociation as an autonomous symptom rather than solely a consequence of trauma. However, the origins and correlates of FND remain unclear. Limited research has examined how dissociation interacts with broader psychological factors, including mood, cognitive flexibility, social support and resilience, or how these variables contribute to the variability in dissociation scores among individuals with FND. Investigating such relationships is critical for the advancement of theoretical models and informing targeted interventions for functional impairments in FND.

The complex and heterogeneous nature of dissociation in FND lends to the need for exploration of a broad range of psychological factors which may contribute to or mitigate dissociative symptoms and/or experiences. Deficits in cognitive flexibility, the ability to shift thought patterns and adapt behaviour, have been linked to dissociative experiences in conditions like PTSD and borderline personality disorder (Şar et al., 2017). Given that dissociation is thought to involve disruptions in executive control over attentional processes (Edwards et al., 2012), examining cognitive flexibility in FND may provide insight into its role in maintaining dissociative symptoms. The literature shows mixed findings concerning cognitive flexibility in those with FND compared to healthy controls (e.g., Pick et al., 2023; de Veroge et al., 2021); such conflicts warrant further investigation. Similarly, rumination, characterised by repetitive and intrusive thoughts, has been associated with heightened psychological distress and prolonged symptom persistence (Ehring & Watkins, 2008; Scott et al., 2019), suggesting that individuals with FND who experience elevated dissociation may exhibit ruminative tendencies. This would have implications for long-term mental health and wellbeing and influence treatment effectiveness.

In addition to cognitive factors, affective processes such as anhedonia (the diminished ability to experience pleasure) may play a role in dissociation. Dissociation has been linked to emotional numbing and detachment (Butler et al., 2021; Pettorruso et al., 2020). Anhedonia is a predictor of poor psychosocial functioning and has implications for long-term physical and mental health, treatment effectiveness and cortex connectivity (Lambert et al., 2018; Vinckier et al., 2017; Young et al., 2016). Given the established association between anhedonia and conditions such as depression and PTSD, its potential relationship with dissociative symptoms in FND warrants further investigation.

Beyond individual psychological processes, social factors may also influence dissociation in FND. Social isolation has been associated with increased dissociative symptoms, potentially exacerbating feelings of disconnection from oneself and others (Gilmartin et al., 2013; Tolmunen et al., 2007) and leading to social disorientation. In comparison, social support may serve as a protective factor by fostering emotional regulation and reinforcing a sense of self-coherence (Korol et al., 2008; Wong et al., 2006). In other studies, this effect was particularly seen as a coping tool for health anxieties and predicting outcomes during the COVID-19 pandemic (Kozosvari et al., 2023). Social isolation/exclusion is often experienced by those with long-term chronic illnesses (Cacioppo & Hawkley, 2003; Dalenberg & Carlson, 2012). However, it is unclear whether this relates to Dissociation in FND.

Finally, resilience, the ability to adapt to adversity, and hopefulness, which is linked to lower psychological distress and improved recovery outcomes (Alayarian, 2019; Loewenstein, 2018; Thomson, 2022) are often related to social isolation and social support and may provide an explanation for varying reports of dissociation in FND. Such variables may provide a buffer against dissociative tendencies, and incorporation of these potential protective factors is essential for a holistic investigation in this area. Investigating such potential protective factors and their relationship to dissociation could inform targeted therapeutic inventions aimed at improving psychologist wellbeing and symptom management in FND and ensure that research drivers, like the current study, consider the applied nature of their findings.

While previous research has explored dissociation in FND largely through the lens of trauma and adverse life events, the role of cognitive, affective and social factors remains unclear. My prior research (Studies 1 and 2 of Blanco et al., 2023) found no significant relationships between adverse experiences, trauma or mood and elevated levels of dissociation

in the FND group, highlighting the need to explore alternative mechanisms underlying dissociation in this population. To address this gap, the present study examines the relationship between dissociation and a broader range of psychological correlates (cognitive flexibility, rumination, anhedonia, social isolation, social support, resilience and hopefulness) in individuals with FND.

This study and data have been collected during COVID-19 restrictions, a unique period during which all participants, regardless of health status, experienced elevated levels of social isolation. This provides a unique context to explore the role of social and psychological factors in dissociation while minimising external variability in social contact. Including a long-term conditions (LTD) control group alongside a healthy control group allows for more nuanced differentiation between dissociation-specific mechanisms in FND and the broader effects of chronic illness symptoms and illness-induced isolation. Given that psychological distress and social challenges are common across long-term health conditions, this additional control group ensures that any identified dissociation-related patterns are not solely attributable to the general experience of living with a chronic condition.

By adopting a multifactorial approach, this research seeks to refine theoretical models of dissociation in FND and contribute to the identification of key mechanisms underlying symptom persistence. The findings may have important implications for understanding the heterogeneity of dissociation and informing targeted investigations that address cognitive, emotional and social factors contributing to symptom severity and maintenance.

5.2.1 Aims and Hypotheses

Through online cross-sectional research, the current study aims to establish whether dissociation is a prominent feature in FND (a finding which could distinguish it from other, similar long-term conditions) and to identify whether usual explanatory factors (mood, social isolation, social support, hopefulness, resilience and rumination) can adequately explain these levels of dissociation in FND. The study also aims to understand the relationship between anhedonia, cognitive flexibility, rumination and resilience. More specifically, the association between implicated triggers for FND and the presence of dissociation is investigated, as well as potential outcomes, with four primary aims: i) to assess whether dissociation is a prominent, defining feature of FND; ii) to test relationships between mood (anxiety, depression and stress),

anhedonia and the presence of dissociation, iii) to test whether dissociation might be associated with social isolation, social support, or resilience which may occur in FND as a result of chronic illness and quality of life changes common in FND, iiii) and finally, to explore the potential effects of heightened dissociation, including correlations with rumination, cognitive flexibility and hopefulness. To address these research aims, scores will be correlated between an FND group, a healthy control group and a long-term conditions group.

In addition, dissociation was explored with reference to Anhedonia, as this emotional detachment could account for an inability to self-identify and, therefore, report mood scores in the FND cohort. The study used scales different from those previously tested to ensure that results were not reliant upon specific psychometric measures and sought to understand dissociation in FND with a range of previously unexplored measures that could act as ACES in dissociative experiences.

The hypotheses for the current study are:

- Those with FND will show higher levels of dissociation than the two control groups (Healthy control and LTD), and those in the long-term conditions group will show higher dissociation levels than those in the healthy control group.
- Scores for anxiety, depression and stress will positively correlate with dissociation scores in each of the three groups (FND, Healthy and LTD), and mood scores (Stress, Anxiety and Depression) will be higher for those in the FND group than the healthy and LTD groups.
- Levels of social isolation and loneliness will positively correlate with dissociation in the three groups (FND, Healthy and LTD), and self-reported social isolation scores will be higher for those with FND.
- Levels of resilience and higher levels of social support will act as a protective factor in dissociation and correlate negatively with dissociation scores.
- Higher levels of rumination will be associated with greater dissociation in all groups, with the strongest relationship expected in the FND group.
- Lower cognitive flexibility scores will be associated with higher dissociation levels in all three groups, with the strongest effect in the FND group.
- Higher levels of hopefulness will correlate negatively with dissociation scores, acting as a protective factor in all groups.

5.3 Methods

5.3.1 Participants

Participants (N = 542; 158 males, 382 females, 2 gender fluid) participated in an online questionnaire. Eighty-two participants were removed from the subsequent analysis as they had >10 % data missing or were deemed to be outliers in preliminary analysis (11 cases had a score exceeding the critical value obtained via Mahalanobis distance, and after examination of individual cases by response pattern these cases were excluded; see Statistical Analyses subsection for further details). The final sample comprised FND participants (N = 163; $Mage$ = 43.41, SD = 12.79), healthy controls (N = 202; $Mage$ = 35.11, SD = 14.17) with no long-term or physical health conditions and a long-term disability control group (LTD; N = 129; $Mage$ = 37.51, SD = 12.52). Participants were recruited through online advertisements on established social media platforms and email circulars distributed via relevant advocacy groups, charities and health communities. The recruitment strategy aimed to ensure accessibility across a broad demographic and particularly targeted FND and LTD groups through patient-led organisations and online communities. All participants provided informed consent before participation and were required to be 18 years or older.

5.3.2 Design

The current study is an online cross-sectional design using a volunteer (unpaid) cohort. Participants with FND were recruited through advertisements with charitable organisations and support groups. Controls (healthy participants with no pre-existing mental or physical health conditions) were recruited through existing online platforms and snowballing. A long-term disability (LTD) group was formed as an additional control. LTD had conditions characterised by similar physical impairments to those with FND, which had lasted for >6 months. To recruit the LTD group, several support groups that supported people with symptoms similar to those with FND shared the study link. Respondents and percentages of those in the LTD group included Fibromyalgia (19.37%), ME/CFS (16.28%), Mood disorders (including bipolar, depression, anxiety, psychosis; 10.08%), Epilepsy (8.53%), Arthritis (8.53%), Ehlers Danlos Syndrome (EDS; 8.53%), Dystonia (various; 7.75%), Lupus (5.42%), Heart and Blood

Disorders (various; 3.88%), Traumatic Brain Injury (TBI; 3.88%), Cancer (Various; 1.55%), Multiple Sclerosis (MS; 3.10%), Other/Non Specific (3.10%).

Much of the sample consisted of UK participants; the demographic variables for each cohort are provided in the studies below. All participants were over the age of 18 and reported being fluent in the English language. Whilst additional demographic information would have added to the strength of the data collected, additional data regarding demographics (including SES, education and employment status) proved challenging to collect and analyse robustly and, thus, are not described within the manuscript. Data were collected using an online survey collection platform (Qualtrics), and an anonymous link was distributed to participants. Results were analysed using IBM SPSS V.24.

5.3.3 Self-Report Scales

5.3.3.1 Anhedonia

Anhedonia was measured using the Dimensional Anhedonia Rating Scale (DARS; Rizvi et al., 2015), a 17-item self-report measure designed to evaluate an individual's interest, motivation, effort and consummatory pleasure across four distinct domains: 1) hobbies, assesses engagement and pleasure derived from activities such as reading, sports or creative arts (e.g., "In the past week, how much pleasure have you experienced from your hobbies?"), 2) Food and drink, evaluates enjoyment related to eating and drinking (e.g., "In the past week, how much pleasure have you experienced from eating your favourite foods?"), 3) Social activities, assessing how much pleasure is obtained from interactions with others (e.g., "How much pleasure have you experienced, in the past week, from socialising with friends or family?") and 4) Sensory experiences, assessing enjoyment of sensory stimuli including music and nature (e.g., "In the past week, how much pleasure have you experienced from listening to music?". The items capture anticipatory and consummatory aspects of pleasure, ensuring the scale provides a nuanced measure of hedonic processing deficits. Participants rated each item on a 5-point Likert scale (0 = not at all to 4 = very much), with higher scores indicating greater hedonic capacity and lower scores reflecting higher levels of anhedonia. The total DARS score was obtained by summing responses across all items, yielding a possible range of 0 to 68. While subscale scores can be calculated separately to assess anhedonia in each domain, this did not apply to the current research scope, and total scores were relied upon.

The DARS has demonstrated strong psychometric properties in both clinical and non-clinical populations. Internal consistency reliability has been reported as excellent (Cronbach's alpha = 0.92; Rizvi et al., 2014), with subscale reliabilities ranging from 0.75 to 0.92, indicating strong consistency across domains. Test-retest reliability studies have shown moderate to high stability over time, with a reported coefficient of r = 0.77 across a three-week period in adolescent samples (Rajeh et al., 2022). The scale also exhibits strong convergent validity, correlating well with established measures like the Snaith-Hamilton Pleasure Scale (Snaith et al., 1995 in Gorostowicz et al., 2023) and the Temporal Experience of Pleasure Scale (TEPS; Gard et al., 2006 in Gorostowicz et al., 2023). Additionally, the DARS demonstrates good divergent validity, showing weaker associations with measures of anxiety, which supports its specificity in assessing anhedonia rather than general distress (Gorostowicz et al., 2023). The scale has been validated for use across various psychiatric conditions, including major depressive disorder and Schizophrenia (Gorostowicz et al., 2023; Rizvi et al., 2014), where it effectively distinguishes individuals with clinical anhedonia from healthy controls. Given its robust psychometric properties and the multidimensional nature of anhedonia assessment, the DARS (Dispositional Anhedonia Rating Scale) is a well-validated tool for evaluating reward processing in diverse populations. Its sensitivity to changes in hedonic experience and its ability to distinguish various sub-facets of anhedonia make it particularly valuable for research investigating the psychological mechanisms underlying various affective disorders and related conditions. In this study, the DARS was selected due to its comprehensive assessment of anhedonia across multiple domains, alongside strong evidence of reliability and validity. This makes it an appropriate measure for examining the relationship between anhedonia and dissociative symptoms in Functional Neurological Disorder (FND). The internal consistency of DARS in the current study was assessed using Cronbach's alpha, yielding a reliability coefficient of 0.88, indicating strong internal consistency within this sample.

5.3.3.2 Anxiety and Stress

Anxiety and stress levels were assessed using the Depression, Anxiety and Stress scale (DASS-21; Lovibond & Lovibond, 1995), a 21-item self-report instrument designed to measure negative emotional states across three domains: depression, anxiety and stress. Each subscale comprises seven items, with responses rated on a 4-point Likert scale ranging from 0 (did not apply to me at all) to 3 (applied to me very much or most of the time). In the current study, only the Anxiety and Stress subscales were utilised.

The anxiety subscale evaluates autonomic, arousal, skeletal muscle effects, situational anxiety and subjective experiences of anxious affect. Sample items include “I was aware of the dryness of my mouth” and “I experienced breathing difficulty, breathlessness in the absence of physical exertion”. The stress subscale assesses difficulty in relaxing, nervous arousal and being easily agitated, irritability, reactiveness and impatience. Sample items include “I found it hard to wind down” or “I tended to over-react to situations”. Scores for each subscale were calculated by summing the relevant items and multiplying by two, as recommended by the authors, to align with the original DASS-42 scoring system. This adjustment ensures comparability across studies and facilitates interpretation (Lovibond & Lovibond, 1995). The decision to focus on the Anxiety and Stress subscales stems from their relevance to the study’s objectives. Anxiety is characterised by the physiological hyperarousal and fear responses, while stress pertains to persistent tension and irritability. Both constructs are pertinent when examining emotional dysregulation and its impact on psychological well-being (Gloster et al., 2009; McTeague & Lang, 2013). Notably, the DASS-21 differentiates between these constructs, allowing for nuanced assessment (Ali et al., 2021; Gloster et al., 2009; Henry & Crawford, 2011).

The DASS-21 has demonstrated robust psychometric properties across diverse populations (Gloster et al., 2009). Studies have confirmed its construct validity, with factor analyses supporting the three-factor structure corresponding to depression, anxiety and stress. The anxiety and stress subscales, particularly, have shown high internal consistency with Cronbach’s alpha coefficients typically exceeding 0.80 (e.g., Antony et al., 1998; Henry & Crawford, 2011; Pezirkianidis et al., 2018). Furthermore, the DASS-21 exhibits strong convergent validity, correlating significantly with other established measures of anxiety and stress. Its ability to discriminate between clinical and non-clinical groups underscores its utility as both a clinical and research tool. In the current study, the internal consistency of the Anxiety and Stress subscales was evaluated, yielding Cronbach’s alphas of 0.85 and 0.88, respectively, indicating strong reliability within this sample. Given its brevity, ease of administration, and solid psychometric foundation, the DASS-21 is well-suited for assessing stress in clinical and research settings.

5.3.3.3 Depression

Depression was assessed using The Beck's Depression Inventory-II (BDI-II; Beck, Steer & Brown, 1996), a 21-item self-report instrument designed to evaluate the severity of depressive symptoms in adolescents and adults aged 13 and above. Each item corresponds to a specific symptom of depression, encompassing affective, cognitive, somatic, and vegetative dimensions aligning with DSM-IV criteria for major depressive disorder. Participants rate each item on a 4-point Likert scale ranging from 0 (symptom absent) to 3 (severe symptom), reflecting on their experiences over the past two weeks. Total scores are calculated by summing the ratings for all items, yielding a possible range of 0 to 63, with higher scores indicating greater symptom severity. The following cut-off scores are typically used to interpret the BDI-II results: 0 – 13 (minimal depression), 14 – 19 (Mild depression), 20 – 28 (Moderate depression), 29 – 63 (Severe depression). In non-clinical populations, scores above 20 are often considered indicative of depression.

The BDI-II has demonstrated robust psychometric properties across diverse populations and clinical settings (Gebrie, 2018; Dotson et al., 2019; Waseem, 2017). It exhibits high internal consistency with reported Cronbach's alpha values ranging from 0.89 to 0.94 (Beck, Street & Brown, 1996); Wang & Gorenstein, 2013), supporting its reliability as a measure of depressive severity. Test-retest reliability over a one-week interval has been found to be r = 0.93, indicating strong stability over time (Wang & Gorenstein, 2013). The BDI-II also demonstrates convergent validity, correlating highly with established clinical measures of depression, including the Hamilton Depression Rating Scale (HDRS; r = 0.71) and the Patient Health Questionnaire-9 (PHQ-9; r = 0.89; Richter et al., 1998; Aranu et al., 2001).

However, despite its strong psychometric profile, concerns have been raised regarding its applicability across racial and neurodiverse populations. For example, research involving African American and Caucasian university students found no evidence of racial bias in BDI-II scores (Sashidharan et al., 2012). Similarly, a study examining midlife women of African descent across various regions in the US supported the BDI-II's factor structure within these populations (Gary et al., 2018). However, other authors note that certain culturally influenced symptom expressions may not be adequately captured by the BDI-II (Forkmann et al., 2018), and there is some evidence of differential item functioning across ethnic groups (Grothe et al., 2005). Furthermore, in neurodiverse populations, particularly in those with autism, cognitive processing differences may alter responses to self-report measures of depression, leading to under or overestimation of symptoms (Cassidy et al., 2018). The scale therefore may not be

specific enough or effective when considering a range of populations (Dotson et al., 2019; Tureson & Thames, 2022). For example, some research indicates that autistic adults may interpret certain BDI-II items differently, potentially affecting the accuracy of depression assessments in this group (Williams et al., 2021). Despite these critiques, the BDI-II is still widely used and often considered less problematic compared to other assessments of depression, including DASS-21, which may conflate symptoms of depression, anxiety and stress, leading to less precise assessments and other measures which do not consider the cognitive correlates of depressive symptoms. As such, it should be noted that findings may need consideration of cultural factors, particularly when interpreting the BDI-II.

The decision to utilise the BDI-II in the current study was based on several key considerations. Firstly, it provides a broad and more nuanced assessment of depressive symptoms covering affective, cognitive, somatic and vegetative dimensions, whereas others (like DASS-21) focus primarily on affective and somatic symptoms (Lovibond & Lovibond, 1995). Given the current study's focus on cognitive aspects of depression, the BDI-II places greater emphasis on these areas, including self-critical thoughts and hopelessness, which better aligns with the study's objectives (Whisman et al., 2000). The BDI-II has been extensively validated in both clinical and non-clinical populations and across multiple demographic groups (Beck et al., 19996; Wang & Gorenstein, 2013) and is more specific in distinguishing symptoms. This is particularly needed in populations where mood disorders and somatic symptoms frequently occur, including in FND (Henry & Crawford, 2005). Though the BDI-II has been critiqued for potential cultural and neurodiversity-related limitations, it remains a more cognitively oriented measure. To mitigate such bias in the current study, pilot studies were conducted to assess clarity in instructions to reduce potential misinterpretation of questions by neurodiverse participants. There was also an allowance of open-text responses for participants who wished to elaborate on their symptom experiences, and scores were cross-referenced with qualitative responses for additional clinical indicators where needed and available. Within the current study, the scale showed good internal reliability (Cronbach's alpha = 0.94).

5.3.3.4 Social Isolation

As this data was collected during the COVID-19 pandemic restrictions, social isolation was assessed using the Social Isolation Scale (Cotton et al., 2017). This concise, 3-item self-

report measure evaluates the extent of an individual's social isolation by focusing on their perceived connections and interactions with others. Participants responded to each item using a 5-point Likert Scale ranging from 1 (strongly disagree) to 5 (strongly agree), with higher scores indicating greater levels of social isolation. An example item from this scale is "I feel isolated from others". These items are designed to capture the subjective experience of social isolation, reflecting feelings of detachment and lack of social engagement. This was particularly important in the COVID-19 restrictions as there could have been differing levels of restrictions globally at the time of data collection, and there was individual subjectivity concerning the impact of the restrictions imposed.

The Social Isolation Scale has demonstrated good internal consistency, with a reported Cronbach's alpha of 0.83 (Cotton et al., 2017), indicating a reliable measurement across diverse populations. The inclusion of the measure in this study served to assess participants' perceived isolation during the unique context of COVID-19 restrictions specifically. It is essential to distinguish between social isolation and social support, representing related but distinct constructions. Social isolation refers to the objective lack of social interactions, contacts and relationships with family, friends and the community (Manera et al., 2022). It encompasses both the absence of social networks and the limited frequency of social engagements. On the other hand, social support is about the emotional, instrumental, informational and companionship provided. It pertains to the subjective perception and actuality of being cared for and valued as part of a social network. By measuring social isolation, the current study aimed to capture the extent to which individuals were physically and emotionally detached from their social networks, which is pertinent during periods of enforced social distancing. This is distinct from assessing social support, which is about the quality and availability of supportive relationships regardless of the frequency of social interactions. Understanding the degree of social isolation is a critical construct in relation to dissociation as both involve experiences of detachment that can impact mental health, and prolonged feelings of social isolation may exacerbate or trigger dissociation (Cacicoppo et al., 2016). The inclusion of this measure provides valuable insights into the potential impacts of reduced social contact on mental health outcomes in the context of pandemic-related restrictions.

5.3.3.5 Social Support

Social support was assessed using the OSLO Social Support Scale-3 (OSSS-3; Meltzer, 2003), a concise instrument designed to evaluate individuals' perceived social support level. The OSLO-3 comprises three items which assess the number of close confidants, interest and concern from others, and ease of obtaining practical help. An example item from the scale is "How much interest and concern do other people show in what do you?". The total score is calculated by summing the responses, yielding a range from 3 to 14. Higher scores indicate greater levels of social support. This scale has demonstrated satisfactory psychometric properties across various studies (Zhang et al., 2024), including internal consistency scores of 0.60 in a Nigerian student sample and 0.69 in a Chinese nursing student sample, indicating acceptable reliability given the scale's brevity (Kocalevent et al., 2018). A student reported a retest coefficient of 0.907, suggesting excellent stability over time (Zhang et al., 2024), and factor analyses in these studies supported a one-factor solution, accounting for approximately 58.54% to 61.56% of the variable. This indicates that the three items collectively measure a single underlying construct of social support.

The inclusion of the OSLO in this study is justified by its brevity and efficiency; its concise format minimises respondent burden,2 making it suitable for inclusion in a comprehensive survey design without compromising data quality or adding to participant fatigue. OSLO has been identified as a strong predictor of mental health outcomes, including psychological distress and depressive symptoms, underscoring its relevance in assessment in studies which include mental health correlates (Kocalevent et al., 2018). The scale has been utilised and validated in diverse cultural contexts, enhancing generalisability across different populations and, in this study, is ideal for capturing social networks' functional aspects. The scale showed good psychometric properties and good internal validity in the current study (Cronbach's alpha = .71).

5.3.3.6 Rumination

Rumination was assessed using the Ruminative Response Scale (RRS; Treynor et al., 2003). This later development by Treynor et al. (2003) was designed to focus on two distinct subcomponents: brooding and reflection (Parola et al., 2017). Brooding represents a maladaptive form of rumination characterised by passive comparison of one's current situation with unachieved standards (Parola et al., 2017; Ruiz et al., 2017). Whereas reflection can

denote a more contemplative form of rumination, involving purposeful turning inward to engage in cognitive problem-solving to alleviate a problem. The refined 10-item scale evaluates individuals' habitual responses to feelings of sadness or depression with each item rated on a 4-point Likert scale ranging from 1 (almost never) to 4 (almost always). Higher scores indicate greater tendencies toward rumination. In this study, both the brooding and reflection subscales were utilised, while items overlapping with depressive symptoms were excluded to prevent redundancy following the recommendations by Treynor et al. (2003).

The RRS has demonstrated robust psychometric properties across various populations (Townshend & Hajhashemi, 2023). Internal consistency is acceptable as denoted by a Cronbach's alpha of 0.77, and test-retest reliability has been satisfactory over time with coefficients ranging from 0.60 to 0.80 across different intervals (Trynor et al., 2003). The RRS was selected for this study because of its ability to differentiate between maladaptive and potentially adaptive forms of rumination. This distinction is crucial for understanding the nuanced roles that different ruminative processes play in psychological constructs like depression, anxiety and dissociation. By employing the RRS, the study aims to explore how brooding and reflection differentially relate to dissociative symptoms in FND and contribute to a more comprehensive understanding of the cognitive processes underlying FND.

5.3.3.7 Resilience

Resilience was assessed using the Brief Resilience Scale (BRS; Smith et al., 2008), which conceptualises resilience as the individual's capacity to recover from stress and adapt to challenging circumstances. The BRS consists of six items, with three positively worded (e.g., "I tend to bounce back quickly after hard times") and three negatively worded (e.g., "I tend to have a hard time making it through stressful events") statements. Participants rate each item on a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree). Negatively worded items are reverse-scored, and the mean of all six items is calculated to derive the overall resilience score, with higher scores indicating greater resilience.

The BRS has demonstrated robust psychometric properties in previous work with the original study citing Cronbach's alpha of 0.80 to 0.91 across different samples, indicating strong internal consistency. The unidimensional factor structure of the BRS has been supported in various studies, including cross-cultural validations, confirming that the scale effectively measures a single construct of resilience. The BRS was selected for use in the current study

due to its focus on resilience as the ability to bounce back from stress, aligning with the study's interest in differences in coping mechanisms among different populations compared to those with FND (Smith et al., 2008). Its brevity and strong psychometric properties make it a practical and reliable tool for assessing resilience in clinical and non-clinical populations. Additionally, the BRS has been evaluated as one of the most frequently used resilience scales, demonstrating satisfactory psychometric properties (Windle et al., 2011). The scale showed good psychometric properties in the current study, corroborating the single-factor solution with internal consistency and validity (Cronbach's alpha = .83).

5.3.3.8 Hopefulness

Hopefulness was assessed using the Perceived Hope Scale (PHS: Krafft et al., 2019), which measures an individual's positive expectations about the future, particularly in contexts where coping mechanisms may be challenged. The PHS consists of six items, such as "Hope outweighs anxiety in my life", rated on a 6-point Likert scale ranging from 0 (strongly disagree) to 5 (strongly agree). Higher scores indicate greater levels of perceived hope. The scale has shown good internal consistency with Cronbach's alpha values ranging from 0.87 to 0.89 in previous studies, indicating this as a reliable measurement. Factor analyses have supported the unidimensional structure of the PHS, confirming that the six items effectively measure a single construct of perceived hope (Krafft et al., 2019). The PHS has been validated in various cultural contexts, including German and Arabic-speaking populations, demonstrating its adaptability and relevance across different demographic groups (Fekih-Romdhane et al., 2025).

The PHS was selected for this study due to its concise format, strong psychometric properties, and focus on the subjective experience of hope. These characteristics make it a practical and reliable tool for assessing hopefulness in clinical and non-clinical populations. Additionally, the PHS has been utilised as part of the World Health Organization's Quality of Life measures, underscoring its relevance and acceptance in assessing psychological constructs related to well-being (Krafft et al., 2019).

5.3.3.9 Cognitive Flexibility

Cognitive flexibility was assessed using the Cognitive Flexibility Inventory (CFI), developed by Dennis and Vander Wal (2010), to evaluate an individual's capacity to adapt their thinking and behaviour in response to changing situational demands. The CFI comprises

20 items, each rated on a 7-point Likert scale ranging from 1 (strongly disagree) to 7 (strongly agree), with higher scores indicating greater cognitive flexibility. Within the CFI is the subscale alternatives, which assesses the ability to perceive multiple and alternative explanations to generate multiple alternative solutions to difficult situations (Kurginyan & Osavolyuk, 2018) and control, which measures the tendency to perceive difficult situations as controllable. The original study reported a Cronbach's alpha of 0.91 when used as a total scale, indicating high internal consistency. The CFI has also shown good stability over time with a 7-week test-retest reliability coefficient of 0.75 for the total score (Kurginyan & Osavolyuk, 2018). The CFI correlates significantly with measures of coping strategies and depressive symptomology, supporting its convergent validity.

While the CFI is a widely used self-report measure of cognitive flexibility, certain limitations do need to be acknowledged. As with all self-report instruments, responses can be influenced by social desirability and lack of self-awareness, and the accuracy of the assessment in online surveys cannot be guaranteed. Further, although the CFI has been translated and validated in various languages, cultural differences in interpreting items may impact its cross-cultural applicability (Kurginyan & Osavolyuk, 2018). Some studies have found weak divergent validity from measures of anxiety and depression, suggesting that the CFI may not fully distinguish cognitive flexibility from related constructs (Johno et al., 2014). Despite these limitations, the CFI was selected for this study due to its strong psychometric properties and its focus on cognitive processes relevant to coping and adaptability. Understanding cognitive flexibility is particularly pertinent to the study of FND, where adaptability in thinking may influence symptom management, dissociative tendencies and overall functioning.

5.4.3.10 Dissociation

Dissociation was assessed using the Multiscale Dissociation Inventory (MDI), developed by Brière, Weathers & Runtz (2005), which evaluates dissociative experiences across six distinct subscales: Disengagement, Depersonalisation, Derealisation, Emotional Constriction, Memory disturbance, and Identity Dissociation. The MDI comprises 30 items, rated on a 5-point Likert scale ranging from 1 (never) to 5 (very often), with higher scores indicating greater levels of dissociation. In addition to subscale scores, the MDI provides a total dissociation score, reflecting the overall severity of dissociative symptoms (Brière, 2002).

The MDI has demonstrated strong psychometric properties across various populations with high internal consistency (Cronbach's alpha = 0.96), indicating excellent reliability. The MDI correlates significantly with other measures of dissociation and trauma-related symptoms, supporting its convergent validity while also distinguishing dissociation from unrelated constructs, affirming its discriminant validity (Jeffirs et al., 2023). Confirmatory factor analyses support the six-factor structure of the MDI, aligning with theoretical conceptualisations of dissociation as a multidimensional construct (Brière, Weathers & Runtz, 2005; Van der Hart & Dorahy, 2022).

The MDI was selected for this study due to its comprehensive assessment of dissociative phenomena, moving beyond unitary models to encompass a range of dissociative experiences. This multidimensional approach aligns with contemporary conceptualisations of dissociation, as discussed in Chapter 2, and it is particularly relevant in the context of FND, where dissociative processes are considered central to symptomology. Concerns regarding the potential overlap between MDI items and FND symptoms are acknowledged. However, the MDI is designed to broadly assess dissociative experiences rather than specific FND symptoms. This distinction is crucial as it allows for the differentiation between dissociative processes and the manifestation of FND symptoms, thereby enhancing the specificity of the assessment. Moreover, research indicates that dissociation in FND is associated with more severe functional symptoms and poorer quality of life, underscoring the importance of assessing dissociation as a distinct construct in this population (Campbell et al., 2022). The selection of the MDI reflects its robust psychometric properties and alignment with the study's objectives to comprehensively assess dissociative experiences and potentially related constructs in individuals with FND.

5.3.4 Procedure

Data for this study was collected between April and June 2020, at a time when large sections of the population were forced to limit social interaction and travel due to the COVID-19 pandemic. This provided an opportunity to study social isolation and its relationship with dissociation in FND, using a unique social situation in which people, regardless of health status, experienced similar restrictions to social movement. After providing informed consent, participants provided demographic information and answered a battery of psychological self-

report measures before being debriefed. Data was collected using Qualtrics, a widely used platform for designing, distributing, and analysing surveys in various research fields. Participants accessed the survey through a secure link provided by the researcher.

5.3.5 Ethics

The University's College Research Degrees Committee (CRDC) provided ethical approval for the following studies. Research standards and practices were followed as outlined by the British Psychological Society (BPS), especially guidelines pertaining to online mediated research (British Psychological Society, 2013).

5.3.6 Power and Sample Size

Given that the proportion of missing data is directly attributed to the quality of statistical inferences, participants were removed from the analysis if they had >10 % missing data (whilst not a commonly applied rule, Bennett (2001) states that statistical analysis is more likely to be biased beyond this threshold). Given the equal importance of sample size and quality of the data, a priori power analysis was conducted using G*Power version 3.1.9.7 (Faul et al., 2007), which generates minimum sample size requirements based on effect size, error probability, degrees of freedom, number of groups and covariates. Results indicated the required sample size to achieve 80 % power for detecting a medium effect, at a significance criterion of a = 0.05, was N = 225 for MANOVA global effects. G*Power suggested a minimum sample size of 55 participants per group in an independent samples t-test. The minimum recommended sample sizes were exceeded in all studies (post-data removal, based on missing values). Effect sizes were calculated by Eta Squared and interpreted based on Cohen's (1988) cut-off values, and confidence intervals have been reported at 95 %.

5.3.7 Statistical analyses

Preliminary analyses were performed to assess the assumptions of normality, linearity, homogeneity of variance-covariance matrices and multicollinearity. No scale or subscale was

excluded because the data was not normally distributed. To screen for multivariate outliers amongst the variables in each of the three studies, Mahalonobis distance scores were generated from multiple regression analyses. Mahalanobis distance follows a Chi-square (x2) distribution, in which the degrees of freedom are equivalent to the number of independent variables in the model (Tabachnick et al., 2007). In the current study, there were 7 degrees of freedom, which equated to a critical Chi-Square value of 24.32 (at $a = 0.001$). Mahalonbis-distance tests indicated eleven cases with a distance score exceeding this critical value. After examination of the individual cases by response pattern and parameter estimates, these cases were deemed to be abnormal based on the populations from which they were drawn. Thus, given this and their sufficiently large influence on the regression parameters, these eleven cases were excluded from the subsequent analyses. The normality of variables was also assessed using the Shapiro-Wilk test, which indicated a violation of the assumption of normality for all variables. However, given the large sample size and skewness and kurtosis values of between -2 to +2 for each of the scales and subscales, this violation was not considered problematic.

To protect against inflating Type 1 error, MANOVAs with follow-up ANOVAs and post-hoc comparisons were applied. Pearson correlations between the dependent variables showed correlations mostly within the moderate range (.02 - .60; Myers et al., 2019); the meaningful pattern of correlations observed among most of the dependent variables validated the appropriateness of using MANOVA in this study. Additionally, Box's M value was 133.411 ($p = .009$), interpreted as non-significant. Thus, the covariance matrices between the groups were assumed to be equal for the purposes of MANOVA. Prior to conducting follow-up ANOVAs, the homogeneity of variance assumption was tested for all subscales of Dissociation. Based on a series of Levene's F tests, the homogeneity of variance assumption was considered satisfied ($p < .05$). However, there were two instances where this was not the case; Levene's F test suggested that the variances associated with the dissociation subscales Identity and Depersonalisation were not homogeneous. An examination of the standard deviations revealed that none of the largest standard deviations were more than four times the size of the smallest, suggesting that the ANOVA would be robust enough to handle this (Howell, 2012).

Finally, multicollinearity was assessed using tolerance and VIF and Durbin-Watson statistics for the assumption of independent errors, which explores serial correlations and tests whether adjacent residuals were correlated. Tolerates were deemed accepted with a value of all tolerances >0.1, VIF values <10 and Durbin-Watson values between 0 and 4 (=1.95).

After tests of assumptions, MANOVA was used to compare scores between the *Groups* (FND, Long-term other conditions (LTD) and Healthy) on Anhedonia, Anxiety, Depression, Social support, Social Isolation, Stress, Resilience, Hopefulness, Rumination and Cognitive Flexibility. Pearson's Correlations tested for the relationship between these variables in relation to dissociation. Fisher's *Z*-tests were computed to compare the magnitude of these correlations between the three groups.

5.4 Results

Table 1 shows the descriptive statistics, t/f-values and significance for the groups for anhedonia, anxiety, depression, social isolation, social support, loneliness, resilience and dissociation.

Table 1: Means, standard deviations, Cronbach's alpha and significant values of each of the tested variables for the three groups (Study 1)

	FND		LTD		Controls		*Skewness*	*Kurtosis*	∝	*f statistic*	*95% CI*	*p*
Variables	x̄	*SD*	x̄	*SD*	x̄	*SD*						
Anhedonia	64.49	12.46	69.02	10.45	70.19	9.05	-.89	1.23	**.88**	12.696	[.0182, .0948]	**<.001**
Anxiety	10.32	5.57	9.40	4.77	7.37	5.54	.20	-.88	**.93**	13.125	[.0193, .0969]	**<.001**
Depression	14.33	13.64	21.81	12.12	25.27	10.64	.51	-.36	**.94**	34.635	[.0775, .1874]	**<.001**
Social Isolation	5.70	2.08	6.39	1.94	6.75	1.99	-.11	-1.24	**.83**	11.682	[.0157, .0896]	**<.001**
Social Support	8.43	2.34	8.86	2.29	9.45	2.03	.03	-.58	**.71**	8.877	[.0092, .0747]	**<.001**
Stress	7.98	5.83	6.10	4.71	3.73	4.23	.80	-.25	**.93**	30.257	[.0662, .1721]	**<.001**
Rumination	22.24	7.66	21.06	6.67	19.31	7.11	.43	-.64	**.90**	6.679	[20.188, 21.518]	**.001**
Resilience	2.66	0.84	2.89	0.79	3.33	0.79	-.04	-.55	**.87**	28.610	[2.887, 3.037]	**<.001**
Hopefulness	16.42	7.45	15.55	7.09	19.65	5.45	-.37	-.43	**.93**	16.194	[18.636, 20.661]	**<.001**
Cognitive Flexibility	92.51	18.53	96.45	13.93	101.63	14.58	-.16	.51	**.89**	13.069	[95.465, 98.399]	**<.001**
Dissociation (Total)	66.64	25.9	56.64	21.76	48.86	20.73	1.18	.81	**.96**	24.823	[.0505, .1495]	**<.001**
Disengagement	15.74	5.19	14.12	5.29	12.43	4.81	.25	-.75	-	17.452	[.0305, .1176]	**<.001**
Identity	7.52	4.52	6.88	3.63	6.89	3.98	1.92	1.89	-	1.271	[.0000, .0236]	.281
Emotional	11.41	6.20	10.36	5.93	8.28	4.95	.94	-.38	-	12.880	[.0186, .0957]	**<.001**
Memory	11.53	5.55	9.18	4.62	7.49	3.82	1.18	.63	-	30.516	[.0662, .1720]	**<.001**
Depersonalisation	9.96	5.60	7.73	3.68	6.65	3.54	1.70	1.91	-	23.889	[.0479, .1456]	**<.001**
Derealisation	10.48	5.45	8.37	4.59	7.11	4.11	1.51	1.36	-	21.026	[.0401, .1335]	**<.001**

Note: Cronbach's alpha scores under the '∝' columns are bolded if deemed to be >0.7 and thus show good internal reliability. Significance is listed under 'p' column with sign and significant effects are bolded. In rows, interactions have been detailed along with relevant significant values. '-' has been used to represent where data was not available i.e. when testing was not conducted as it was not applicable to the interaction or when this test was not conducted.

5.4.1 Mood

There was a significant effect of *Group* for Anhedonia [f (2,457) = 12.70, p <.001, ηp^2= .05, small effect], Anxiety [f (2,457) = 13.13, p <.001, ηp^2=.05, small effect], Depression [f(2,457) = 34.64, p <.001, ηp^2=.13, moderate effect] and Stress [f (2,457) = 30.53, p <.001, ηp^2=.12, moderate effect]. Compared to healthy controls, the FND group showed significantly lower scores for anhedonia (p <.001), anxiety (p <.001) and depression (p <.001). The FND group has significantly higher stress scores than healthy controls (p <.001). In comparison to the LTD group, the FND group showed significantly lower scores for anhedonia (p = .001) and depression (p <.001). The FND group showed significantly higher scores than the LTD group for stress (p<.001). There were no significant differences between the FND and LTD groups for anxiety (p =.308).

5.4.2 Dissociation

There was also a significant difference in dissociation scores between the three groups [f (2,457) = 24.823, p <.001, ηp^2 = .098, moderate effect]. Significantly higher mean scores were seen in the FND group than in the LTD group (p = .001) and the healthy control group (p <.001). The mean score of the LTD group was also significantly higher than the mean score for the healthy control group (p = .011); however, the greatest difference was between the FND and Control groups ($\bar{x}dif$ = 17.78, p <.001).

Further analysis showed this effect was present for most of the 6 subscales of dissociation: the FND group scored significantly higher than the LTD group for Disengagement (p = .019), Memory (p <.001), Depersonalisation (p <.001) and Derealisation (p = .001). The FND group also scored significantly higher than healthy controls for Disengagement (p <.001), Emotional (p <.001), Memory (p <.001), Depersonalisation (p <.001) and Derealisation (p =.001). The LTD group showed significantly higher scores than healthy controls for Disengagement (p = .014), Emotional (p <.001), Memory (p = .007), and Depersonalisation (p = .009). The subscale Identity did not show any statistically significant differences between the groups; there were no other noteworthy significant interactions.

5.4.3 Social Isolation and Social Support

There was a significant effect for *Group* for social isolation [f (2,457) = 11.68, p <.001, ηp^2 = .05] and social support [f (2,457) = 8.88, p <.001, ηp^2= .04]. Post-hoc tests showed lower scores for social isolation in the FND group compared to the Healthy group (p = <.001) and lower scores in the FND group compared to the LTD group (p = .009). LTD and the healthy group (p = .297) showed no significant difference in social isolation scores. Significantly lower scores were reported by the FND group in social support compared to the healthy control group (p = <.001). There were no significant differences in social support between the FND and LTD group (p = .226) or between the LTD and healthy group (p = .06).

5.4.4 Hopefulness, Rumination and Resilience

There was a significant effect for *Group* for Hopefulness [f (2,457) = 16.194, p = <.001, ηp^2= .066], Rumination [f (2,457) =6.679, p = .001, ηp^2= .029] and Resilience [f (2,457) = 28.610, p = <.001, ηp^2= .112]. Post-hoc comparisons showed that Hopefulness scores were significantly lower in the FND group in comparison to the Healthy group (p <.001) and significantly lower in the LTD group compared to the Healthy group (p <.001). Similarly, Rumination was significantly higher in the FND group than in the Healthy group (p = <.001), and Rumination scores were significantly higher in the LTD group in comparison to the Healthy group (p = .038). There were no significant differences between the FND and LTD groups for Hopefulness (p = .270) or Rumination (p = .187). Resilience, however, showed significantly lower scores in the FND group compared to the Healthy group (p <.001) and compared to the LTD group (p = .017). Resilience scores were also significantly lower in the LTD group compared to the healthy group (p <.001).

5.4.5 Cognitive Flexibility

There was a significant effect for *Group* for Cognitive flexibility [f (2,457) = 13.069, p = <.001, ηp^2= .054]. Post-hoc comparisons showed significantly lower scores for the FND group compared to the LTD group (p = .047) and significantly lower scores for the FND group compared to the Healthy group (p <.001). There was also a significant difference between the LTD and Healthy group for Cognitive Flexibility (p = .006).

5.4.6 Relationships to Dissociation

Table 2 shows Pearson's Correlation Coefficients for Anhedonia, Anxiety, Depression, Stress, Dissociation, Social Support and Social Isolation separated by *Group*. In those with FND, Dissociation showed statistically significant, weak, negative correlations with Anhedonia [p = .001, 95% CI [-.4054, -.1166]] and Social Support [p <.001, 95% CI [-.4993, -.2307]]. There were strong positive correlations in the FND group with Dissociation for Anxiety [p <.001, 95% CI [.521, .713]], Stress, [p<.001, 95% CI [.5762, .7496]] and Depression [p<.001, 95% CI [.6052, .7688]]. There was a weak, positive correlation between Dissociation and Social Isolation [p <.001, 95% CI [.1318, .4182]]. A similar pattern of results is seen in both the LTD and Healthy groups, with Dissociation showing strong positive correlations with Anxiety (p <.001), Stress (p <.001), and Depression (p<.001). Correlations between Anhedonia and Dissociation in the LTD and Healthy groups were not significant. Both the Healthy and LTD groups showed a weak negative correlation between Dissociation and Social Support (p <.001) and a weak positive correlation between Dissociation and Social Isolation (p <.001).

Pearson's were also explored for Hopefulness, Rumination, Resilience, and Cognitive Flexibility, and these correlations are presented, separated by *Group*, in addition to those above in Table 2. Of note, in those with FND, Dissociation showed a statistically significant, strong positive correlation with Rumination [p <.001, 95% CI [.5342, .7196]]. There were moderate negative correlations in the FND group with Dissociation for Resilience [p <.001, 95% CI [-.5653, -.3174]], Hopefulness [p <.001, 95% CI [-.5781, -.3344]] and Cognitive Flexibility [[p <.001, 95% CI [-.5573, -.3077]]. A similar but somewhat reduced pattern of results was seen in the Healthy and LTD groups, where there was a moderate positive correlation between Dissociation and Rumination in both groups (p <.001). There were weak, significant, positive correlations with Dissociation and Resilience (p = .002), Hope (p <.001) and cognitive flexibility (p <.001) in the LTD and Health Groups.

Table 2: Correlations between dissociation, anhedonia, anxiety, stress, depression, social isolation, social support, hopefulness, rumination, resilience and cognitive flexibility in the FND, LTD and Healthy Groups (Study 1)

Group	**Variables**	Anhedonia	Anxiety	Stress	Depression	Social Isolation	Social Support	Hopefulness	Rumination	Resilience	Cognitive Flex	Dissociation
FND	Anhedonia	1										
	Anxiety	-.134	1									
	Stress	-.125	.809**	1								
	Depression	-.329**	.704**	.724**	1							
	Social Isolation	-.024	.467**	.437**	.529**	1						
	Social Support	.155*	-.229**	-2.56*	-.343**	-.207**	1					
	Hopefulness	.399**	-.414**	-.440**	-.677**	-.364**	.331**	1				
	Rumination	-.090	.716**	.691**	.759**	.383**	-.269**	-.465**	1			
	Resilience	.377**	-.431**	-.462**	-.619**	-.295**	.263**	.600**	-.515**	1		
	Cognitive Flex	.402**	-.413**	-.482**	-.557**	-.297**	.179*	.512**	-.350**	.518**	1	
	Dissociation	-.261**	.617**	.663**	.687**	.275**	-.365**	-.465**	.636**	-.450**	-.441**	1
LTD	Anhedonia	1										
	Anxiety	-.009	1									
	Stress	.116	.752**	1								
	Depression	-.126	.693**	.592**	1							
	Social Isolation	.013	.301**	.338**	.352**	1						
	Social Support	.127	-.245**	-.175*	-.386**	-.293**	1					
	Hopefulness	.146	-.484**	-.401**	-.693**	-.158	.412**	1				
	Rumination	.028	.630**	.656**	.502**	.369**	-.250**	-.380**	1			
	Resilience	.069	-.569**	-.476**	-.577**	-.112	.321**	.612**	-.410**	1		
	Cognitive Flex	.195*	-.373**	-.337**	-.370**	-.166	.322**	.397**	-.356**	.390**	1	
	Dissociation	-.102	.514**	.531**	.586**	.259**	-.358**	-.297**	.506**	-.272**	-.305**	1
Healthy	Anhedonia	1										
	Anxiety	-.054	1									
	Stress	.015	.733**	1								
	Depression	.052	.710**	.615**	1							
	Social Isolation	.008	.470**	.393**	.512**	1						
	Social Support	.106	-.272**	-.245**	-.396**	-.278**	1					
	Hopefulness	.032	-.302**	-.337**	-.446**	-.306**	.242**	1				
	Rumination	.118	.715**	.604**	.776**	.453**	-.202**	-.405**	1			
	Resilience	-.20	-.363**	-.376**	-.409**	-.163**	.144	.430**	-.426**	1		
	Cognitive Flex	.163*	-.366**	-.436**	-.366**	-.259**	.310**	.434**	-.273**	.497**	1	
	Dissociation	.139	.462**	.679**	.582**	.329**	-.277**	-.364**	.586**	-.268**	-.379**	1

Note: ** highlights that correlation is significant at the .001 level.

To ascertain whether the magnitude of the correlations between the psychometric measures differed significantly between the three groups (FND, LTD and Healthy), 10 Fisher's Z-Tests for multiple independent samples were conducted, followed by independent comparisons of correlation coefficients (using Fisher's Z transformations where appropriate). Results revealed that the strength of the correlation between *Dissociation* and *Anhedonia* was significantly different between the FND (z = -.27), LTD (z = -.10) and Healthy (z= .14) Groups [$x^2(3) = 15.04$, $p = .001$]. Results also revealed that the strength of the correlation between Dissociation and Cognitive Flexibility was significantly different between the FND (z = -.473), LTD (z = -.315) and Healthy (z = -.399) Groups [$x^2(3) = 11.34$, $p = .01$]. The magnitude of the difference was not significant for *Dissociation* and the following: *Anxiety* (p=.112), *Depression* (p = .195), *Stress* (p = .095), *Social Anxiety* (p = .760), *Social Support* (p =.590) *Rumination* (p = .167), *Hope* (p = .173).

5.5 Discussion

The present cross-sectional project aimed to establish the relationship between dissociation and FND and explore several factors implicated in the development of dissociation that could influence this relationship. Specifically, measurements included: i) comparisons in dissociation between those with FND, LTD and Healthy controls; ii) relationships between mood (anxiety, depression and stress), anhedonia and the presence of dissociation; iii) relationships between dissociation with social isolation, social support, or resilience which may occur in FND as a result of chronic illness and quality of life changes common in FND, iv) and the potential effects of heightened dissociation, including relationships with rumination, cognitive flexibility and hopefulness.

The findings of this study support previous work (e.g. Blanco et al., 2023; Campbell et al., 2023; Pick et al., 2020) and support the notion that elevated dissociation in FND is heightened relative to both healthy controls and those with other long-term illness, on most subscales (Derealisation, Memory/gaps, Emotional, Disengagement and Depersonalization) but not on those focusing on identity. The findings in previous work in this field do not support a relationship between dissociation and trauma or dissociation and mood in FND (Blanco et al., 2023). The current study shows no discernable relationship between mood and dissociation or social isolation and dissociation in FND. This suggests that elevated dissociation may be

particularly prominent in FND and greater than in other similar chronic illnesses, thus corroborating previous assertions that dissociative tendencies are a significant difficulty for those diagnosed with FND (Brown et al., 2007; Pick et al., 2017). For example, those with FND are also known to have greater susceptibility to dissociation induction in laboratory studies (Perez et al., 2018) and are susceptible to detachment and compartmentalisation phenomena (Brown et al., 2007; Holmes et al., 2005). Dissociative symptoms are not commonly reported in other conditions like CFS/ME, fibromyalgia, Ehlers-Danlos Syndrome, Multiple Sclerosis and others which made up the LTD group in the current study and which have overlapping cognitive or neurological symptoms to FND. Such findings help to identify the main areas of dysfunction in FND, with implications for focusing interventions and future research. Understanding dissociation in FND could be valuable in refining treatment options and increasing focus on overcoming dissociation, in combination with grounding and body or emotion-focused techniques, such as eye movement desensitisation and reprocessing (EMDR; Cope, 2020) and mindfulness-based therapies (Baslet et al., 2020). Whilst the effectiveness of EMDR and mindfulness-based theories is not controversial, further studies should investigate their effectiveness at reducing dissociation in FND and their potential effectiveness at reducing symptoms.

Investigations here sought to understand if heightened dissociation in FND is associated with being chronically ill (and concomitant life changes) or a product of mood. The current findings suggest dissociation in FND is higher than in both healthy controls and in those with other long-term health conditions whose symptoms mimic FND. Thus, high dissociation scores appear to be a key feature in FND and more prominent than in conditions with similar symptoms. Given the high variability of dissociation in the FND group, it is possible that dissociation may be particularly associated with certain subtypes, such as Functional Seizures (Goldstein & Mellers, 2006); Functional Seizure subtypes are also associated with raised dissociation compared to those with epilepsy (Myers et al., 2019). Identification of such FND subtypes, characterised by dissociation, might have implications for tailoring treatment for FND. Dissociation was associated with higher disability scores in previous work (Blanco et al., 2023) and could reflect generally higher disability and impairment to quality of life than those with other organic disorders (Carson et al., 2011).

In the current data, there was no association between dissociation and social isolation in FND. Moreover, even during global social isolation (this study was conducted during the COVID-19 pandemic), FND participants maintained higher dissociation than both control

groups. This is particularly interesting as it could be argued that those with FND may be more accustomed to social isolation and restrictions to their movement as a result of the unpredictability of symptoms and reduced quality of life.

Both the LTD and FND groups reported higher anxiety during this period, although this might reflect a lack of access to medical or support care for their conditions during "lockdown". This might reflect not only social isolation but also broader anxieties related to the pandemic itself. Beyond these concerns around access to medical or support care, individuals with chronic illnesses and disabilities faced heightened distress due to public health policies, such as the controversial "do not resuscitate' (DNR) orders that disproportionately targeted disabled populations. Additionally, fears surrounding COVID-19 infection and its potential long-term effects on pre-existing conditions may have further contributed to elevated anxiety levels. Vaccine hesitancy or concerns about the safety and efficacy of rapidly developed vaccines, particularly in those with complex or poorly understood health conditions, may have also played a role in heightened distress. At this time, many prominent physicians and societies in the FND community needed to give statements on vaccine effectiveness and potential contraindications.

Given these findings, I recommend that future research continues to explore the importance of dissociation in FND. Further, given the lack of evidence here (and in my previous research) to support that elevated dissociation is a product of usual triggering factors (mood, adverse life experiences and social isolation) it should be considered if dissociation in FND is a symptom of the illness itself rather than a reaction to external stresses. If so, further investigation is needed to understand what, if any, biopsychosocial mechanism triggers such elevated levels and if this is a key indicator which distinguishes FND positively from other related conditions.

When those with FND are compared to others (with or without long-term conditions) who are being subjected to the kinds of social isolation that often accompany FND, we still find elevated dissociation in people with FND. This suggests that elevated dissociation in FND is likely not attributable to the social isolation the patients endure as a result of their chronic illness. Notably, the FND group reported less anhedonia than the other two groups, which might indicate prior habituation with the isolation conditions that affected the other groups more strongly. The discrepancy between previous findings and our own could reflect differing methodologies and sample acquisition; I recruited participants through advertisements on FND

support groups, whereas prior literature more heavily relies upon patients in either neurological or psychiatric clinics or meta-analyses. Alternatively, disruption to the typical dissociation-ACEs relationship in FND might reflect a reluctance to report adverse life events due to a sensitivity/awareness of stigma. However, this alternative explanation is somewhat speculative and needs to be explored in further studies. Thus, based on the current results, I argue that high dissociation scores in FND do not have a relationship with adverse life experiences (Blanco et al., 2023). Future research should explore the extent to which adverse life events increase susceptibility to developing FND across symptom subtypes.

Additional potential correlates of dissociation were also explored through this work, including Hopefulness, Resilience and Rumination. Rumination is widely recognised as holding a relationship to dissociation, particularly Depersonalisation and Derealisation and is a strong predictor of dissociation and adverse effects like reduced sleep quality, reduced cognitive flexibility and decreased coping and emotion regulation (Cavicchioli et al., 2021; Ródenas-Perea et al., 2023; Slater et al., 2005; Vannikov-Lugassi et al., 2018). Whilst higher rumination levels have been identified in Functional Seizure Subtypes (Konovalova, 2023), the findings presented in the current study suggest that there is no increased rumination in FND when compared to other long-term illnesses. Whilst both illness groups in the current study (FND and LTD) display increased rumination relative to controls, this could indicate having chronic illness more generally rather than being a trait specific to FND. A similar pattern was seen for Hopefulness in the current study. Previous literature suggests that hopefulness may relate to dissociation but may also indicate self-stigma in illness experienced (Prasko et al., 2016, 2017). Hopefulness has been studied in FND in relation to treatment outcomes (Cope, 2020) but not in a more general sense in FND. Again, the findings presented here suggest that there are no differences between those with FND and those with other long-term conditions but that both groups show reduced hopefulness in comparison to healthy controls. By contrast, Resilience scores in the current study were significantly different in all three groups and were the lowest in those with FND. Whilst the reason for these results can only be speculated, resilience has previously been linked to other psychological correlates of FND including alexithymia (Jalilianhasanpour et al., 2018) and is thought to be reduced as being a product of dealing with increased stress, and the unknown in FND (Canna & Seligman, 2020; Kozlowska et al., 2023). Correlations with dissociation were found in the current study for Hopefulness, Resilience and Rumination. While the study found these correlations across all three groups, the FND group presents with the strongest correlations. This may indicate that these constructs

amplify dissociative experiences in FND, but they are certainly not indicative of these constructs as causal factors explaining elevated dissociation in FND.

Cognitive Flexibility was significantly different between the three groups (FND, LTD and Healthy), with the FND Group reporting the lowest scores for this construct. Due to the differences in reported scores between those with other long-term conditions and FND, the finding may suggest that reduced cognitive resources and fixed mindsets may be more common in those with FND. Previous research certainly supports this finding as cognitive flexibility has been consistently found to be a primary cognitive deficit in FND (Alluri et al., 2020; de Vroege et al., 2021; Teodoro & Edwards, 2018) and this may influence other cognitive symptoms and hinder treatment progression, particularly with forms of psychological therapies (Arbuthnott, 2020; Graham et al., 2028). Cognitive Flexibility also held a strong correlation with dissociation in the FND group, and post-correlation comparisons revealed significant differences between all groups in this regard, with FND reporting the largest correlation. This indicates a likely relationship between dissociation and cognitive processes in FND, which are distinctly different to those with other long-term conditions, and this finding warrants further exploration.

This study is not without its limitations, namely the use of self-report measurements of psychological constructs collected remotely with individuals self-identifying their health status. At the time of data collection, methods of online screening of FND were limited, and thus, participants with FND were asked to confirm that they had i) been given the diagnosis of FND from a neurologist and ii) had experienced symptoms for more than 6 months. Those with other Long-term conditions (control group) were asked to provide similar information as well as naming health conditions. The presence of comorbid physical and mental health diagnoses and the use of medications may influence the findings in the FND group. However, symptom-pure groups are unlikely in this condition and given that the studies here repeatedly demonstrate high dissociation, this influence seems unlikely. Future studies should, however, also aim to explore if dissociation subtypes and levels influence symptoms in FND and illness outcomes. However, despite these limitations and across different and large samples of patients with FND this pattern of elevated dissociation remains and warrants further exploration and incorporation into theoretical models and the provision of treatment. One additional limitation of the present study is the lack of characterisation of the LTD control group, particularly regarding the extent of functional restrictions and symptom burden experienced by participants. While the LTD group was included to provide a comparison with individuals managing chronic health

conditions, it remains possible that differences in family life restrictions, symptom severity, or coping mechanisms could contribute to dissociation levels. Future research would benefit from systematically matching the LTD group to the FND group, based on some given variables such as functional impairment, pain severity, fatigue levels and emotional distress, to ensure that observed differences in dissociation are not attributable to broader effects of chronic illness. By refining group comparisons in this way, future studies could further delineate the unique role of dissociation in FND, distinguishing it from dissociation associated with chronic illness more broadly.

5.6 Chapter Summary

The current study demonstrates raised dissociation in FND, relative to healthy individuals and those with other long-term chronic health conditions. Understanding mechanisms underpinning dissociation in FND would have implications for the development of etiological models and may be key to the disorder in general. Based on the present findings, dissociation in FND does not appear to be associated with adverse life events or mood (stress, anxiety and depression) or psychosocial adversity (social isolation). Dissociation was, however, associated with increased levels of anhedonia and decreased levels of cognitive flexibility in those with FND but not in those with other long-term conditions. Future studies should look towards identifying any biological correlates of dissociation in FND. This raises the need to address the potential mediating role of dissociation throughout the remaining empirical studies in this thesis as a potential mediating factor influencing symptoms. Chapter 7 builds upon this further to explore the relationship between dissociation and brain function, particularly as the work here suggests that there is a strong relationship between dissociation and cognitive flexibility in FND.

This chapter also raises the question of whether there are differences in the nature of dissociation across FND subtypes and if the variable nature of this construct could, in part, explain the variability in symptom presentation in FND. This is further explored in Chapter 6, which aims to explore the potential relationships between symptoms and triggers in FND and if symptom types may vary in their experience of dissociative subtypes.

Chapter 6: Subtypes of FND: A Latent Class Analysis

6.1 Chapter Overview

The previous chapters have explored contemporary conceptualisations of FND and demonstrated key psychological correlates which could distinguish FND from other disorders, including dissociation and its effects on Cognitive Flexibility. Throughout the literature, there is a general assumption that underlying mechanisms may be the same across all FND subtypes (Kola & LaFaver, 2022; Nicholson et al., 2020). However, there are repeated calls for the need to distinguish FND subtypes and clinical findings indicative of similar risk factors (Kola & LaFaver, 2022) but different symptom and neurobiological profiles (Aybek et al., 2022; Matin et al., 2017; Perez et al., 2021). Some have identified possible trauma subtypes of FND (Paredes-Echeverri et al., 2022) and possible motor (Aybek & Perez, 2022; Matin et al., 2017) and cognitive subtypes (Alluri et al., 2020; Kemp et al., 2022; Lamer, 2021; Paredes-Echeverri et al., 2022; Teodoro et al., 2018). Only one paper to date has attempted to explore possible relationships to symptom outcomes using empirical data (Butler et al., 2021), despite this being a recognised clinical phenomenon (Lidstone et al., 2021; Keynejad et al., 2019). Evidence suggests that there may be physical and biopsychosocial factors which contribute to the development of the disorder and trigger symptoms (Geroin et al., 2022; Jungilligens et al., 2020). Therefore, the current Chapter aims to advance this understanding further and explore a broader range of potential predisposing factors to see if these hold a relationship with the FND subtype. Firstly, the work re-tests the concepts of dissociation, mood and cognitive flexibility in those with FND as being distinct from healthy controls and other long-term conditions. Comparisons are also made in other measures, including burnout, quality of life and illness triggers. This empirical work also aims to demonstrate possible subtypes of FND through cluster analysis and explore if these are predicted by predisposing or precipitating factors. It also aims to explore the relationship between these symptom clusters and additional "non-core" symptoms of FND (such as pain and fatigue) and dissociation.

6.2 Introduction

As a name, FND conveys ideas of a condition produced by alterations of functioning in neural networks rather than structural alterations. Throughout the literature, FND is described as a product of its symptoms, a notion that seems contradictory and, at times, too all-encompassing. Current diagnostic criteria allude to a multitude of symptoms experienced by those with FND in a 'catch-all' diagnostic category, one that is too broad and creates further conceptual confusion (Ball et al., 2020; Hallet et al., 2022; Gupta & Lang, 2009; LaFrance et al., 2013; Staab et al., 2017). Those with FND can be afflicted by a range of symptoms, including alterations in motor, sensory or cognitive performance and distressing deficits, which can occur as constant (continual) deficits or with variability. This raises the question of a unitary diagnosis as it is likely that there are different phenotypes (Stone et al., 2004); individuals may present with one (or more than one) or alternate between phenotypes of FND (Hallett et al., 2022; Lidstone et al., 2021; Nicholson et al., 2020). Whilst it has previously been suggested that there are likely shared pathologies and physiological underlying mechanisms across FND subtypes (Bennett et al., 2021; Fobian & Szaflarksi, 2021; Milano et al., 2023; Pick et al., 2024), this argument has long been used to support the notion of studying FND subtypes together. More recently, there have been calls from clinicians to begin to distinguish between FND Subtypes (Hallett, 2022; Fiorio et al., 2022); whether symptom subtypes have underlying commonalities on a neurophysiological level remains unknown (Voon et al., 2016), as reviewed throughout Chapter 3.

Aetiological work has highlighted that there is a possible role of the precipitating factor in determining specific functional neurological symptoms and other related, non-core symptoms; in some cases, clear evidence has been presented, particularly between the nature of the physical precipitant and subsequent phenomenology of symptoms (Stone et al., 2019). However, the physical precipitants identified in this work (including minor injury, flu, and migraine) are very common in the general population, and why these would trigger FND in a small proportion of people remains unexplained. Whilst some have suggested that predisposition may play a role, including genetic factors (Spagnolo et al., 2020) and other biological predispositions (Apazoglou et al., 2018; Maurer et al., 2016), these predispositions may still not be specific to the development of FND, to distinguish its pathology from other neurological disorders. Other work has highlighted that structural illness or injury may also predispose someone to particular FND subtypes. For example, Epilepsy may predate functional

seizures (Kutlubaev et al., 2018), and migraine may precede the development of Functional Limb Weakness (Tinazzi et al., 2021). Some neurological disorders are known to be more likely to trigger FND than others, including Parkinson's Disease over, for example, Alzheimer's Disease (Walzl et al., 2019), which may precede Functional Movement Disorder and be a result of specific impacts on motor neural networks. Investigations of this phenomenon must, therefore, account for mechanistic factors in the development of FND as well as biopsychosocial factors. Understanding the link between precipitating and predisposing factors and their potential connection to subsequent FND symptoms or phenotypes remains a crucial area of investigation of continued relevance and importance.

The diverse array of neurological symptoms that seemingly still lack a clear structural or organic cause can lead to significant impairments in a patient's daily functioning and overall quality of life. The intricate interplay between psychological and neurological factors in FND necessitates a comprehensive examination of various constructs, including dissociation, mood disturbances, burnout, cognitive flexibility and quality of life to understand better and begin to classify symptom subtypes within his population. Some of these constructs were previously explored in Chapter 5 but are again assessed here to explore if these experiences can exacerbate FND symptoms or support the classification of FND subtypes. For example, mood disturbances, such as anxiety and depression, are prevalent in FND. However, these affective symptoms may not only contribute to the overall burden of the disorder but may also influence the severity and manifestation of neurological symptoms (Kanner et al., 2003). Burnout (characterised by emotional exhaustion and reduced personal accomplishment) may also arise in FND patients as a precursor to their symptoms or as a result of the chronic stress and persistent nature or unpredictability of symptoms. Many authors also stress that Quality of Life is markedly diminished in FND, reflecting the pervasive impact of the disorder on physical, emotional and social functioning (McWhirter et al., 2024; Paredes-Echeverri et al., 2022; Pick et al., 2020). Measuring Quality of Life in FND studies provides a holistic view of the patient's experience and may prove essential in targeted therapeutic approaches and discerning potential subtypes.

FND can present with several symptoms in varying combinations (Matin et al., 2017), such that work to attempt to understand potential symptom clusters is often problematic. In classification systems, a number of subtypes are proposed, though rarely used in clinical practice. The Diagnostic and Statistical Manual of Mental Health Disorders (DSM-5) offers potential diagnosis for core features of FND proposing the following categories: weakness or

paralysis, swallowing, speech, attacks or seizures, anaesthesia or sensory loss or symptoms (including visual, olfactory or auditory) and a category of 'mixed symptoms' for those with combinations of core symptoms (American Psychiatric Association, 2013). The International Classification of Diseases (ICD-11) includes an additional subtype of FND, "functional cognitive disorder", based on recent research (Pennington et al., 2015; Stone et al., 2015). However, alongside core neurological symptoms there are many physical symptoms (such as pain, fatigue, sleep disturbances, attentional deficits and bowel and bladder dysfunction) in addition to psychological symptoms (including cognitive fog, mood, dissociation, anhedonia and alexithymia) which are reported as having clinical significance in FND (Kranick et al., 2011; Nicholson et al., 2020; Popkirov et al., 2019; Şar et al., 2014; Stone et al., 2010). These have been reviewed in Chapter 2 and have been found to negatively impact clinical outcomes (Gelauff et al., 2014; Glass et al., 2018) and have impacts which are just as, if not more, disabling than the core symptoms recognised by classification systems (Gelauff et al., 2018; Věchetová et al., 2018). Specific epidemiological data and statistical validation of potential subtypes, which incorporate a contemporary understanding of FND and various biopsychosocial-related constructs, are lacking.

Recent work on identifying potential subtypes has focused on reviews (e.g., Hallett et al., 2022) and only a few empirical studies (e.g., Bulter et al., 2021; Shipstone-Sharman et al., 2019). Butler et al. (2021) highlighted many potentially under-recognised symptoms and the presence of multiple-symptom comorbidity, which resulted in higher distress. In this study, symptom conditional probability was calculated. However, it was limited to pairs of symptoms that do not inform the complete picture if multiple symptoms overlap to create potential symptom clusters. Hallet et al. (2022) reviewed four potential symptom types suggesting the presence of functional seizures, functional movement disorders, perceptual postural dizziness and functional cognitive disorder. There are, however, other common manifestations, including sensory disturbances, visual or auditory disturbances and speech disorders, which fall outside of these categories. Further, symptoms can vary in severity (Nicholson et al., 2020), and it would be hard to consider, for example, comparable pathologies for paralysis in the same category as tics, convulsions or reduced coordination. Because of such variability of symptom profiles, other research has failed to distinguish discreet symptom subtypes and failed to demonstrate any relationship between precipitating or predisposing factors and symptom outcomes (Shipstone-Sharman et al., 2019). As a result of such difficulties, many have instead explored FND types independently.

There may be key, identifiable differences across FND subtypes from symptom clusters to differences in precipitating factors. In relation to precipitating factors, patients with Functional Movement or Motor Disorder (FMD) may commonly report more physical events (e.g., injury, illness, or surgery) prior to symptom onset (Geroin et al., 2022). It has also been found that in those with Functional Movement Disorder, there is a higher likelihood of walking difficulties, balance, tremors, spasms and jerks (Butler, 2021). Differences in symptom clusters across functional motor symptoms (as potential discreet functional conditions) have not been identified (Gelauff et al., 2019), and previous cluster analysis studies have also failed to identify movement disorder subtypes (Forejtová et al., 2021). However, this research only explored relationships to demographics, mood, mode of onset, pain and fatigue, and there may be a wider range of symptom clusters to consider. As such, it is likely that those with motor forms of FND may be predisposed to multiple symptom manifestations. In Functional Seizure subtypes, there appears to be a higher likelihood of psychological precipitating factors and mood disorder comorbidities (Popkirov et al., 2019; Reuber et al., 2007), whilst others have noted that there is a much wider range of precipitating factors (Asadi-Pooya et al., 2020). However, the literature suggests that Functional Seizures may have distinct phenotypes as there are a wide variety of clinical manifestations (Aversek & Sisodiya, 2010; Izadyar et al., 2019; Rosemergy et al., 2013), which could differ in predisposing and psychological comorbidities (Asadi-Pooya et al., 2020). At present, shared and distinct aetiological underpinnings between Functional Seizures and Functional Movement Disorder subtypes have not been identified (Millman, 2024). Identification of such differences across FND subtypes would enable better diagnosis and a better understanding of illness pathology and could influence treatment outcomes.

Increasingly, previously considered "subjective" cognitive experiences like dizziness and auditory problems are being classified as FND and may represent a distinct subtype (Campbell et al., 2023). Other authors have called for the incorporation of pain and somatic symptom subtypes of FND in future classifications (Maggio et al., 2020). Migraine, fatigue, and bowel and bladder problems are as common (if not more common) than mood disorders in those with FND (Butler et al., 2021). As these currently lie out of the core features of FND, these are likely missed by previous research and clinical assessment/practice and in the exploration of clusters or subtypes of symptoms (Matin et al., 2017). Other researchers have called for drop attacks (idiopathic momentary loss of consciousness) to be considered as a discreet FND subtype (Revell et al., 2021). Some have called for the consideration of possible trauma

subtypes of FND (Paredes-Echeverri et al., 2022), but this does not account for clinical characteristics and mechanisms or consider those who lack a history of ALEs.

A widely accepted subtype of Functional Seizures exists in the literature, although seizure presentations vary significantly (Hallet et al., 2020). Additionally, emerging research has identified Functional Cognitive disorder as a potential FND subtype, characterised by memory failure and attentional difficulties (Ball et al., 2020; McWhirter et al., 2020a, 2020b; Reuber et al., 2018; Williamson & Larner, 2018). As with other subtypes, variations within Functional Cognitive Disorder have been proposed, including isolated cognitive symptoms, dissociative amnesia, and anxiety-driven presentations (Bhome et al., 2019; McWhirter et al., 2020b; Teodoro et al., 2018). Clearly, there remain important differences between these diverse symptoms and understanding potential subtypes of FND could support the further advancement of knowledge in this field. Despite these efforts, previous research has focused mainly on isolated symptom presentations rather than capturing the broader heterogeneity of FND. Many studies have not systematically examined the interplay between dissociation, mood, burnout, cognitive flexibility, and quality of life, nor have they explored how these factors may differentiate symptom clusters in FND. Interestingly, only anecdotal evidence from clinical practice has also linked trigger type to later FND presentation/symptoms, and very few studies have tried to employ this in a statistically meaningful way. This study addresses these gaps by using latent class analysis to identify potential subtypes of FND, incorporating a wider range of psychological and functional variables to advance the classification and understanding of FND presentations.

6.2.2 Aims and Hypotheses

This study aims to understand the prevalence of core and associated symptoms, comorbidities, and predisposing and precipitating factors in FND based on FND patients' own perceptions of their FND narrative. The main aim is to explore if these can be clustered into meaningful and contextual clusters representing subtypes of FND. An online questionnaire was disseminated to an international sample of FND patients to achieve these aims. Utilising a data-driven approach, this study employs a form of cluster analysis (Latent Class Analysis; LCA) to explore potential FND subtypes in an unbiased fashion. Latent class analysis was applied to a large set of symptoms associated with FND. The intent of these analyses was to elucidate the symptomatic heterogeneity associated with this condition. Latent class analysis was selected as a method due to its usefulness in prior studies of complex traits (e.g., Bucholz

et al. 1996; Eaves et al., 1993; Sullivan & Kendler, 1998). Given the typical conceptualisation of the distinctiveness and possibility of subtypes of FND, a *priori* expectation was that LCA would yield different classifications consistent with theoretical assumptions, though this may not account for graduation in severity in singular dimensions. The aims of the current study were therefore; 1) to explore dissociation, mood, burnout, cognitive flexibility and quality of life in those with FND compared to healthy controls and an LTD control cohort, 2) to explore if subtypes exist in FND which can be characterised by clusters of symptoms using LCA 3) to explore if additional "non-core" symptoms hold a relationship with these clusters 4) to investigate if symptom clusters hold a relationship with the precipitating factor in FND, 5) to explore if dissociation and other characteristics are differentially associated with FND subtypes.

Based on the study aims and existing literature, the following hypotheses are proposed:

- H1: Individuals with FND will exhibit higher levels of dissociation, mood disturbances (anxiety and depression), burnout, cognitive inflexibility, and lower quality of life compared to both healthy controls and the LTD group.
- H2: Latent class analysis (LCA) will reveal distinct FND subtypes, characterised by clusters of symptoms, supporting the heterogeneous nature of FND rather than a singular diagnostic entity.
- H3: Non-core symptoms (e.g., migraine, chronic pain, fatigue) will significantly contribute to the characterisation of FND subtypes, suggesting that symptom clusters extend beyond traditional diagnostic criteria.
- H4: Symptom clusters will be associated with different precipitating factors. Certain FND subtypes will show stronger associations with specific triggers, including physical trauma, viral infections, or psychological stressors, while others may lack an identifiable precipitating event.
- H5: Dissociation, mood disturbances, and cognitive flexibility will differentially associate with FND subtypes, suggesting that psychological and cognitive profiles contribute to symptomatic variation within the disorder.

6.3 Methods

6.3.1 Participants

Participants (N = 1227; 991 females; *Mage* = 41.08, *SD* = 12.97) were recruited. Eight participants were removed from the subsequent analysis due to missing data (>10%). The final cohort comprised, FND participants (N = 746; 618 females, *Mage* = 43.02, *SD* = 13.13), Healthy Controls (N = 303; 247 females, *Mage* = 36.58, *SD* = 10.86) and a long-term disability control group (LTD; N = 131; 99 females, *Mage* = 42.06, *SD* = 14.09). Gender splits were roughly even in each group (females accounting for the largest percentage across all three groups, ranging from 74.8% to 83.7%). A one-way ANOVA revealed a significant difference between the average age of groups [f (2, 1219) = 29.2074, p <.001]. The average age was significantly lower in the Healthy control group compared to the FND group (p <.001) and significantly lower than the LTD group (p <.001). Participants with FND were recruited through advertisements within charities and support groups. Owing to a lack of versatile, reliable self-report screening tools for FND, participants were included if they had received a diagnosis of FND by a healthcare professional and if symptoms had lasted for more than 6 months. Controls (healthy participants with no pre-existing mental or physical health conditions) were recruited through existing online platforms and snowballing.

A long-term disability (LTD) group was formed as an additional control. LTD had conditions characterised by similar physical impairments to those with FND, which had lasted for >6 months. To recruit the LTD group, several support groups that supported people with conditions including Multiple Sclerosis, Ehler-Danlos Syndrome, Epilepsy, ME/CFS, and Fibromyalgia advertised the study link. Participants were asked to provide details of their condition/disability if it lasted more than 6 months and significantly impacted their daily function. The final LTD sample consisted of those with a diagnosis of: Arthritis (Various; 7.63%), Cancer (Various 5.35%), Chronic Migraines (2.29%), Chronic Regional Pain Syndrome (3.82%), Ehlers Danlos Syndrome (EDS; 3.05%), Fibromyalgia (19.08%), Heart and Blood Disorders (Various; 3.05%), Long Covid (5.35%), Lupus (2.29%), ME/CFS (16.79%), Mood Disorders (Various; 8.40%), Multiple Sclerosis (MS; 5.35%), Neurodiverse (including ASD/ADHD; 9.15%), Parkinson's Disease (1.53%), Traumatic Brain Injury (TBI; 6.87%).

Much of the sample consisted of UK participants; the demographic variables for each cohort are provided in Table 3 below. All participants were over the age of 18 and reported being fluent in the English language.

Table 3: Demographic information across three groups and total sample (Study 2, Chapter 6)

	Total sample	FND	LTD	Healthy Control
Total Sample Size (N)	1227	746	131	330
Age				
Age range	18 – 84 years	18 – 84 years	18 – 74 years	18 – 84 years
Age Mean (SD)	41.08 (12.97)	43.26 (13.13)	42.06 (14.09)	36.58 (10.86)
Gender frequency				
Female (%)	991 (80.1%)	618 (82.8%)	99 (75.6%)	247 (74.8%)
Male (%)	210 (17%)	103 (13.8%)	26 (19.8%)	81 (24.5%)
Non-binary (%)	27 (2.2%)	21 (2.8%)	6 (4.6%)	0
Not disclosed (%)	9 (.7%)	4 (.5 %)	0	2 (.6%)
Country				
Australia/ New Zealand	20	19	3	0
Belgium	2	2	0	0
Brazil	1	1	0	0
Canada	16	13	2	1
France	1	1	0	0
Germany	1	1	0	0
Greece	1	0	5	0
Italy	1	1	0	0
Ireland	2	2	0	0
Netherlands	7	4	0	0
Norway	1	1	0	0
Russia	1	1	0	0
South Africa	2	2	0	0
Spain	4	3	1	0
Switzerland	1	1	0	0
UK	1072 (90.7%)	647 (86.7%)	120 (95.2%)	328 (99.4%)
USA	36	35	1	0

6.3.2 Materials

Self-report scales were used in this study. To explore comparable effects in a large sample, all participants across the three groups (FND, LTD and Healthy Controls) were asked to complete self-report scales to assess the constructs of Dissociation, Mood, Burnout, Quality of Life and Cognitive Flexibility. Illness data was collected from the FND and LTD groups, including information about duration, length of diagnosis and illness triggers, if known. Additional data was asked of the FND cohort about their illness, including comorbidities, to allow for descriptive analysis and symptoms for a robust class analysis. Details of the measures are outlined in the subsections below.

6.3.2.2 Dissociation

To measure dissociation as a multi-construct model over a unitary model, Brière, Weathers, and Runtz's (2005) Multiscale Dissociation Inventory (MDI) was used. This assesses dissociation across 6 subscales to emulate contemporary notions of the multifaceted nature of dissociative experiences: Disengagement, Identity, Emotional, Memory, Depersonalisation and Derealisation. This scale unveiled useful findings in the previous empirical study (Chapter 5). The 30-item scale also generates a total dissociation score. The scale showed good psychometric properties and good internal validity (Cronbach's alpha = .96).

6.3.2.3 Mood

The *Depression, Anxiety and Stress Scale* (DASS-21; Lovibond & Lovibond, 1995) is a 21-item scale (7 items each for depression, anxiety and stress). Scores on each of the subscales ranged from 0 (none) to 3 (usually/always). The scale assesses dysphoric mood states including self-depreciation, lack of interest, hopelessness, arousal states and emotional liability to stressors across the subscales. Only the Anxiety and Stress subscales were used in the present study. Summed scores were generated and multiplied by two to match the authors' recommendations. The scale has good psychometric properties (Cronbach's alpha = 0.80).

6.3.2.4 Burnout

The Copenhagen Work and Personal Burnout Inventory is a measure developed to assess the extent to which participants have experienced emotional exhaustion and work-related frustration within the past two weeks (Kristensen et al., 2005). Although initial testing was in psychiatric services, this scale has been applied to a broad range of sectors and contexts (Montgomery et al., 2021). Personal and work burnout subscales were used, consisting of 6 and 7 items, respectively (total items = 13). Personal includes six items rated 1 - 5. Participants responded to three items targeting work-related burnout using a 5-point scale ranging from 0 = "Never" to 4 = "Always". Reverse scoring was applied when needed, and high scores indicated high levels of burnout. The scale has good psychometric properties (Cronbach's alpha = .91).

6.3.2.5 Cognitive Flexibility

The Cognitive Flexibility Inventory (CFI; Dennis & Vander., 2010) is a 22-item scale which provides information about two types of cognition: alternative perceptions (the ability to perceive multiple alternate explanations and solutions to problems) and control (the tendency to perceive difficult situations as controllable). Responses to this self-report scale are measured on a 7-point Likert scale from 1 (Strongly disagree) to 7 (Strongly agree). Items were reverse scored when necessary, and total scores were created from a sum of the items with higher scores indicating greater cognitive flexibility. The scale shows good validity (Cronbach's alpha = .89). As this showed potential as an indicator of cognitive function in previous empirical work (see Chapter 5), it was again utilised here to explore correlates with dissociation in a larger sample and to explore influences of type of dissociation on this variable.

6.3.2.6 Quality of Life

Quality of life was evaluated using the *World Health Organization Quality of Life Scale, Abbreviated Version* (WHOQOL-BREF; Whoqol Group, 1998). Validated across populations, this scale measures satisfaction levels using four subscales: perceptions of physical health, perceptions of psychological health (including self-appraisal of positive and negative emotions), social relationships and environment. The 26 items in the WHOQOL-BREF are

rated on a five-point scale ranging from 1 (very poor/never) to 5 (very good/always), with higher scores denoting better (perceived) quality of life. The WHOQOL-BREF reported good internal consistency with Cronbach's α values for the subscales ranging from 0.69 – 0.89 (Power et al., 1999) and good reliability in other health populations (e.g., Fang et al., 2002; Lin et al., 2007; Mas-Expósito et al., 2011).

6.3.2.7 Symptoms

To perform a suitable analysis to meet the study aims, the choice of symptoms, including an analysis of symptomatic heterogeneity, is critical. An obvious initial consideration was to include the symptoms that define FND in major classification systems; however, this assumes that such criteria are correct and that classification systems are up to date with contemporary findings of this condition and would negate other potentially underappreciated symptomatic differences. Rather, this analysis focused on the analysis of symptoms commonly reported throughout the literature and in contemporary pieces which have aimed to provide an overview of symptoms across FND types. Similar approaches to item selection have been used by others in other illness work (Hickie et al., 1995; Sullivan et al., 2002). As part of this questionnaire, participants were asked about 38 different signs and symptoms that are at least occasionally noted by those with FND. While core FND symptoms such as functional seizures, motor and sensory disturbances and speech impairments are well documented in diagnostic frameworks, a growing body of evidence suggested a growing body of evidence suggests a broader, more heterogenous range of symptoms that are frequently reported by individuals with FND yet remain underrepresented in formal classification systems.

To balance comprehensiveness with empirical grounding, symptom selection was guided by a review of contemporary literature on FND symptomatology and previous studies that have attempted to catalogue common and emerging symptoms across different FND subtypes (e.g., Butler et al., 2021; Revell et al., 2021; Teodoro et al., 2018). To ensure methodological rigor, symptoms were included if they appeared in at least three peer-reviewed studies or were identified as frequently reported in clinical or research-based reviews of FND presentations. This approach aligns with previous illness classification work in conditions with significant symptomatic heterogeneity, such as ME/CFS (Hickie et al., 1995) and Fibromyalgia (Sullivan et al., 2002), where symptom inclusion was similarly based on frequency in research literature rather than strict nosologically informed criteria. Of the 38 symptoms included, approximately

60% were drawn from symptoms explicitly mentioned in formal diagnostic classifications (DSM-5/ICD-11), including functional limb weakness, tremors, gait disturbances, functional seizures, sensory loss, speech difficulties, and dissociative symptoms. The remaining 40% comprised of symptoms frequently reported in FND research and clinical literature but not explicitly listed in diagnostic frameworks, such as, migraine, bowel and bladder dysfunction, cognitive dysfunction, dizziness, tinnitus, and non-epileptic drop attacks (Ball et al., 2020; Maggio et al., 2020; McWhirter et al., 2020). Some symptoms are considered non-core symptoms in FND, such as chronic pain or fatigue, and perhaps they are too broad or non-specific. These 12 symptoms were listed as 'additional symptoms'. They were used as part of an extension analysis to see if this influenced the structure of the subclasses developed within the main study.

Participants with FND were presented with the 38-item symptom list and asked to indicate the extent to which each symptom was part of their unique symptom profile, using a 3-point scale (0 – not at all, 1 – occasionally, 2 – a lot/most of the time). They were then presented with a similar scale for the 12 additional symptoms. Additionally, an open-ended section was provided to allow participants to report symptoms they felt were important but not included in the previous predefined list, ensuring that the breadth of symptom experience was captured.

6.3.2.8 Illness Data

In addition to symptom data described above, all participants in the FND and LTD groups were asked to complete an extensive questionnaire to obtain self-report data on antecedent events (possible precipitating and predisposing factors), medical history, comorbidities and demography. These variables were selected to enable comparative analyses, examining the potential impact of diagnosis and broader health history on symptom expression. Additionally, this data was used to inform subsequent latent transition analysis (LTA), which supported a more nuanced understanding of symptom profiles across proposed subtypes of FND.

The inclusion of precipitating and predisposing factors was informed by an extensive literature review, drawing from studies that have explored the role of biopsychosocial influences as potential risk factors for the development of FND (e.g., Ludwig et al., 2018; Perez et al., 2018; Pick et al., 2020). Medical history variables were selected based on evidence of

increased prevalence of specific conditions and or incidents in medical settings happening prior to the onset of FND including migraine, irritable bowel syndrome, hypermobility spectrum disorders, surgery, head injury, and autoimmune conditions (e.g., Hallet et al., 2020; Kranick & Hallet, 2013; McWhirter et al., 2020). Additionally, to ensure the inclusivity of patient-reported experiences, an open-ended section was included to allow participants to list any additional comorbidities they deemed relevant to their health status. This approach aligns with previous research methodologies in complex conditions, where rigid selection may fail to capture the full breadth of relevant medical factors.

By incorporating both structured and open-ended data collection, the study balances methodological rigor with patient-centred reporting, enabling a comprehensive assessment of illness history. Table 4 provides a full breakdown of included illness data, including symptoms, medical history, and comorbidities.

Table 4: Details of items used to assess core symptoms, additional symptoms and predisposing events in Study 2 (Chapter 6)

Symptoms (Core FND)	Additional Symptoms	Triggers (predisposing events)
S1 Walking Difficulty	A1 Chronic Pain	T1 Cold or Flu
S2 Heaviness one-sided	A2 Persistent Fatigue	T2 Viral Infection
S3 Co-ordination (with objects)	A3 Insomnia	T3 Head Injury
S4 Limbs (dissociation from)	A4 Hypersomnia	T4 Another physical injury
S5 Tingling or numbness	A5 Migraines	T5 Operation/ Surgery
S6 Co-ordination (of Limbs)	A6 Other headaches and facial pain	T6 Childbirth
S7 Reduced movement in limbs	A7 Irritable Bowel Syndrome (IBS)	T7 Traumatic Experience
S8 Paralysis	A8 Anxiety and panic attacks	T8 Stress/ Burnout (Work)
S9 Blackouts/ Functional Faints	A9 Depression	T9 Stress/Burnout (Personal)
S10 Functional Seizures	A10 Chronic Urinary Retention	T10 Childhood Trauma
S11 Moments motionless	A11 Dysfunctional Breathing	T11 Symptoms since childhood
S12 Staring unresponsive	A12 Hearing loss or reduced	T12 None
S13 Functional Tremor		T13 Other conditions first
S14 Functional Dystonia		
S15 Excessive movements		
S16 Facial Spasm		
S17 Tics (Eyes)		
S18 Tics (All)		
S19 Jerks and Twitches		
S20 Drop Attacks		
S21 Pins and Needles		
S22 Limbs Disconnectedness		
S23 Memory (Sequential)		
S24 Memory (everyday)		
S25 Memory (Social)		
S26 Memory (Short Term)		
S27 Memory (words)		
S28 Slurred Speech		
S29 Stutter		
S30 Words (finding the right word)		
S31 Words (mix up)		
S32 Speak with Whisper or Hoarse		
S33 No speech		
S34 Foreign Accent Syndrome		
S35 Swallowing difficulties		
S36 Dizziness		
S37 Vision issues (blurred, double or reduced)		
S38 Light Sensitivity		

6.3.2.9 Software

Data were collected using the online survey platform Qualtrics. Data analysis was conducted using the R statistical computing environment, an open-source software environment for data analysis, visualisation and modelling. Specifically, the latent class

analysis (LCA) was performed using the **poLCA** package in R, which provides tools for fitting latent class models to categorical data.

6.3.3 Procedure

Participants took part in this online research through Qualtrics. After providing informed consent, all participants were asked about their health status and demographic information. All participants, regardless of health status, answered scales related to Dissociation, Mood, Burnout, Cognitive Flexibility and Quality of Life. LTD and FND groups were asked for additional health data, such as any precipitating or triggering health factors, duration and comorbidities. Those with FND were asked further questions related to symptoms. After completing the battery of self-report measures, all participants were thanked for their time and debriefed.

6.3.4 Statistical Analyses

6.3.4.1 Preliminary

Preliminary analyses were performed to assess the assumptions of normality, linearity, homogeneity of variance-covariance matrices and multicollinearity. No scale was excluded as a result of abnormalities in the distribution of data. Outliers were screened for in advance of all analyses and removed prior to analysis. No extreme violations were noted in these preliminary analyses prior to the execution of analysis between groups (using MAONA). However, additional caution is noted in the interpretation of the results owing to the homogeneity of covariance matrices, and these have been noted in the 'comparisons between groups' section. Of note, in preparation for the LCA, additional assumptions of data were checked, and data included in the LCA was categorical. Whilst it would have been good to include dissociation into models, data collected was continuous, though further analysis could be done to explore its inclusion at a later date and this construct was explored as a later correlate instead. LCA assumes that observed categorical variables are conditionally independent within each latent class; thus, once the latent class is known, the observed variables are independent of each other.

This type of exploratory LCA cannot assume this, and thus, careful consideration was given to fit indices (outline below) in the examination of proposed latent classes. Local independence could also not be guaranteed, and at best, the work which follows should be considered as speculative latent class suggestions that warrant further confirmation.

6.3.4.2 Comparisons between groups

To protect against inflating Type 1 error, MANOVAs with follow-up ANOVAs and post-hoc comparisons were applied to explorations of variables between groups. Box's M value was 316.527 (p <.001), which was interpreted as being significant and a violation of homogeneity. Levene's test was also significant across many variables, indicating a violation of the assumptions of homogeneity of variances. Together, these indicate that the variances and covariances of the dependent variables differ across groups. Additional exploration of the data and of Log Determinants showed significant differences in the dispersion of data across groups; particularly noted was a larger difference in the log determinant of the Healthy control Group compared to the FND and LTD groups. This implies that, at least in part, results are influenced by greater variability of scores in illness groups; similar dispersion of scores across the dependent variables could indicate similarities in the nature of illness, symptom profiles or common underlying mechanisms. Nonetheless, because of large fluctuations in sample size between the groups and the particularly large data set, Pillia's Trace was used in the subsequent MANOVAs in line with literature recommendations, owing to the sensitivity of Box's M (Cohen, 2008; Hans-Vaughn, 2016). Pillai's Trace is considered robust to violations of assumptions and tends to perform well even with unequal variances and sample sizes. Additionally, post hoc ANOVA relied upon Welch's ANOVA, which does not assume equal variances. Despite such caution in consideration of preliminary analyses, it is recommended that the MANOVA results be interpreted with caution. MANOVA with Pilla's Trace was used to compare the scores between the *Groups* (FND, Long-term other conditions (LTD) and Healthy Controls) on Dissociation, Mood, Burnout, Cognitive Flexibility and Quality of Life. Post hoc Welch's ANOVAs were used to assess relationships between groups to consider the significance of variability across groups and account for unequal variances and sample sizes.

6.3.4.3 Illness data

As illness data was only comparable between two *Groups* (LTD and FND) ANOVA and descriptive statistics have been applied to this data. This included exploration of differences in illness duration, diagnosis length and comorbidities.

6.3.4.4 Latent Class Analysis

Latent Class Analysis (LCA) was conducted to identify homogeneous subgroups (latent classes) within the FND sample based on reported symptoms, triggers for illness, and additional correlates. LCA is a statistical method used to classify individuals into mutually exclusive and exhaustive groups based on their response patterns to categorical variables (Collins & Lanza, 2010). The principles of latent class analysis were followed (e.g., Eaves et al., 1993; Collins & Lanzza, 2010). This analysis intended to characterise the number and structure of latent classes to understand heterogeneity in FND better. The first goal was to determine the number of latent (i.e. observed) classes that gave rise to the observed data (e.g., the 50 dichotomous physical symptoms associated with FND). Latent classes are not observed directly but instead are inferred from observed data. LCA can give rise to 1 to $2^{38} - 1$, which is approximately 274,877,906,943, or over 274 billion possible unique combinations, if there was a latent class corresponding to each possible unique combination of these 50 symptoms. If more than one class is present, the characterisation of classes can be informed by consideration of theoretical understandings and referenced additional data. This has supported the analysis in identifying distinctive and better-informed latent classes. Consideration was also given to correlates of these classes that may distinguish them, including the nature of the predisposing or precipitating event and dissociation subtypes. Prior to analysis, the dataset was prepared by encoding categorical variables (e.g., symptoms, triggers, dissociation subtypes) as factors in R (R Core Team, 2021). Irrelevant observations were excluded from the LCA analysis, particularly those not corresponding to "Healthy" or "Ill" health statuses.

The LCA model was fitted using the **poLCA** package in R (Linzer & Lewis, 2011). The model included symptoms, triggers, dissociation subtypes, and additional correlates (e.g., cognitive flexibility, anxiety, stress, depression) as predictors of latent class membership. The

number of latent classes was determined based on theoretical considerations and model fit indices, including the Akaike Information Criterion (AIC, a measure of model fit that balances the goodness of fit with complexity wherein lower values indicate better fit) and Bayesian Information Criterion (BCI; which penalises model complexity more heavily than AIC). Sample-size adjusted BIC (aBIC) was not utilised as the sample size of the FND Group (N = 746) exceeds minimum thresholds for LCA (Dziak et al., 2014; Björklund, 2002). Additional model fit indices included the Maximum Likelihood Ratio (MLR), which is commonly used in estimating parameters for LCA, and Entropy as a measure of classification accuracy ranging from 0 to 1 (with higher scores denoting better classification. Upon fitting the LCA model, model parameters were examined to interpret the latent classes with class membership probabilities computed to determine the likelihood of individuals belonging to each latent class. Additionally, variable distributions within each latent class were analysed to characterise the profiles of symptoms, triggers, and correlates associated with each class.

The LTA model thus considers item probability parameters where M represents the class items (indicators, in this case, symptoms) that are observed in individuals (u). The items are assumed to be independent measures of underlying latent class variables (C) which has (K) latent classes. Once a latent class is accounted for, the items are assumed to be independent from one another (known as conditional independence assumption) and observed items are decomposed to be a function of class-specific item probability, specifically:

$$P(u_j = 1) = \sum_{k=1}^{k} \quad P(u_j = 1 | C = k).$$

This equation denotes the probability that an item is one, or the marginal probability. The observed probability is decomposed into the sum of conditional item probabilities that vary by class. The class-specific item probabilities are then expressed as individual thresholds on the inverse logit scale, specifically:

$$P(u_j = 1 | C = k) = \frac{1}{1 + \exp(-\omega jk)}$$

The class size parameters, or class proportions (π_k) are then expressed on the multinomial logistic regression formulation, specifically:

$$\pi_k = P(C = k) = \frac{\exp(\alpha_k)}{\sum_{k=1}^{k} \exp(\alpha_k)}$$

Herein each individual is a member of only one latent class, with item responses assumed to be independent and conditional on class membership. Class size parameters are considered the structural parameters of the LCA model and whilst these are estimated as logits, they are converted to probabilities. These are reported as percentages indicating the degree to which each class accounts for the percentage of the sample.

6.4.3.4 Latent Transition Analysis (LTA)

Owing to model complexity, the LCA was conducted on the initially identified 38 symptoms. However, many of these do not account for other common symptoms seen in the condition, which are considered with growing relevance to the diagnosis and understanding of FND. As such, Latent Transition Analysis (LTA) was used as an extension of LCA to explore the dynamic class groups based on additional symptom information. LTA is also referred to as latent Markov modelling and is an extension of LCA, which can explore the interrelations of multiple latent class variables. LTA allows for the tracking of changes to class membership and the opportunity to reconceptualise latent class variables that may sometimes be otherwise modelled with a static structure (Hagenaars & McCutcheon, 2002; Langeheine, 1988). In this sense, the LCA extracted classes are regressed onto the previously identified structure and denoted by transition probabilities.

6.4.3.5 Further relationships between latent classes

As other collected data was not categorical, it was used as comparative data of the proposed latent classes (FND Subtypes). General linear models or Log Likelihood ratio tests were applied where appropriate to explore the relationship between proposed latent classes and Predisposing event and the relationship between proposed latent classes and Dissociation.

6.4 Results

The study first conducts a MANOVA to compare FND, Healthy, and LTD groups, followed by an exploration of illness-related data within the FND and LTD groups. Subsequently, a Latent Class Analysis (LCA) is conducted within the FND group to identify underlying subgroups, followed by an examination of correlates associated with the identified classes.

6.4.1 Between Group Comparisons

Table 4 shows the descriptive statistics, f-values and significance for the groups for Dissociation Total (and 6 subtypes), Stress, Anxiety, Depression, Burnout, Cognitive Flexibility and Quality of Life.

Table 5: Means, standard deviations, Cronbach's alpha and significant values of each of the tested variables for the three groups (FND, LTD & Healthy) in Study 2, Chapter 6

	FND		LTD		Controls		*Skewness*	*Kurtosis*	∝	*f*	*95% CI*	*p*
Variables	x̄	*SD*	x̄	*SD*	x̄	*SD*				*statistic*		
Anxiety	29.29	9.64	28.59	10.24	21.10	6.97	.677	-.329	**.79**	85.564	[20.08, 22.12]	**<.001**
Burnout	72.46	17.35	61.23	19.14	42.59	19.49	-.452	-.378	**.93**	271.651	[40.53, 44.65]	**<.001**
Depression	30.92	12.15	32.47	12.52	23.05	9.62	.561	-.795	**.84**	53.668	[21.74, 24.35]	**<.001**
Stress	32.03	10.89	32.45	10.64	25.15	8.96	.408	-.745	**.91**	48.133	[.0662, .1721]	**<.001**
Cognitive Flexibility	73.25	5.96	75.03	5.77	77.03	5.36	-.160	-.151	**.89**	19.919	[72.59, 73.90]	**<.001**
Quality of Life	66.91	14.19	72.94	16.41	91.29	13.12	.161	-.730	**.87**	299.427	[89.68, 92.89]	**<.001**
Dissociation (Total)	68.65	20.43	59.91	20.90	44.73	15.84	.937	.777	**.91**	152.386	[42.79, 47.16]	**<.001**
Disengagement	16.01	4.52	14.66	5.85	10.97	4.18	.400	1.023	-	121.383	[10.46, 11.50]	**<.001**
Identity	7.16	4.30	6.44	3.06	5.98	2.46	2.866	8.446	-	10.515	[5.56, 6.41]	**<.001**
Emotional	11.91	4.99	10.07	5.30	7.66	3.97	.986	.339	-	81.177	[7.12, .8.20]	**<.001**
Memory	11.97	5.01	10.20	4.43	7.34	3.29	.937	.254	-	106.296	[6.83, 7.85]	**<.001**
Depersonalisation	10.85	4.36	9.46	4.80	6.35	2.84	1.186	1.058	-	125.822	[5.89, 6.80]	**<.001**
Derealisation	10.75	4.53	9.08	4.59	6.67	2.97	1.237	1.292	-	98.180	[6.20, 7.14]	**<.001**

Note: Cronbach's alpha scores under the '∝' columns are bolded if deemed to be >0.7 and thus show good internal reliability. Significance is listed under 'p' column with sign and significant effects are bolded. In rows, interactions have been detailed along with relevant significant values. '-' has been used to represent where data was not available i.e. when testing was not conducted as it was not applicable to the interaction or when this test was not conducted.

In relation to mood, there was a significant effect of *Group* for Anxiety [f (2, 1025) = 85.564, p <.001, ηp^2=.143, large effect], Depression [f (2, 1025) = 53.668, p <.001, ηp^2= .095, moderate effect], and Stress [f (2, 1025) = 48.133, p <.001, ηp^2=.086, moderate effect]. There were no significant differences between FND and LTD for Anxiety (p = 1.000), Depression (p = .554), or Stress (p = 1.000). There was a significant difference between FND and Healthy groups for Anxiety (p <.001), Depression (p <.001), and Stress (p <.001) with the FND groups reporting higher measures of each. This was emulated in the differences between the LTD and Healthy groups, where the LTD group reported significantly higher measures than the Healthy group for Anxiety (p <.001), Depression (p <.001), and Stress (p <.001).

There was a significant effect of *Group* for measures of life impacts, including Quality of Life [f (2, 1025) = 299.427, p <.001, ηp^2= .396, very large effect], Burnout [f (2, 1025) = 271.651, p <.001, ηp^2= .364, very large effect] and Cognitive flexibility [f (2, 1025) = 19.191, p <.001, ηp^2= .037, moderate effect]. Post-hoc comparisons showed significantly lower scores for the FND group compared to the Healthy control group for Quality of Life (p <.001) and Cognitive Flexibility (p = .002) and higher scores in the FND group compared to the Healthy group for Burnout (p <.001). There were also lower scores for the FND group compared to the LTD group for Quality of Life (p <.001) and Cognitive Flexibility (p = .002) and higher scores in the FND group compared to the LTD group for Burnout (p <.001).

There was also a significant difference in total dissociation scores between the three groups [f (2, 1025) = 152.386, p <.001, ηp^2= .229, large effect]. Significantly higher mean scores were seen in the FND group than in the LTD group (p = .001) and the healthy control group (p <.001). The mean score of the LTD group was also significantly higher than the mean score for the healthy control group (p = .011); however, the greatest difference was between the FND and Healthy Control group ($\bar{x}dif$ = 23.68, p <.001).

Further analysis of dissociation as a product of its 6 subscales showed statistical significance at the *Group* level for all variables with large effect sizes for Disengagement (p <.001, ηp^2= .191), Emotional (p <.001, ηp^2= .137), Memory (p <.001, ηp^2= .172) Depersonalisation (p <.001, ηp^2= .197) and Derealisation (p <.001, ηp^2=.161). There was a significant difference between the three groups for Identity, with a small effect as denoted by partial eta squared (p <.001, ηp^2= .020). Further analysis showed this effect was present for most of the 6 subscales of dissociation: the FND group scored significantly higher than the LTD group for Disengagement (p = .012), Emotion (p <.001), Memory (p <.001),

Depersonalisation (p = .002) and Derealisation (p < .001). The FND group also scored significantly higher than healthy controls for Disengagement (p <.001), Emotional (p <.001), Identity (p =<.001), Memory (p <.001), Depersonalisation (p <.001) and Derealisation (p <.001). The LTD group showed significantly higher scores than healthy controls for Disengagement (p <.001), Emotional (p <.001), Memory (p < .001), Depersonalisation (p < .001) and Derealisation (p <.001). The subscale Identity did not show any statistically significant differences between the FND and LTD groups (p = .173) or the LTD and Healthy group (p = .778), but there were significantly higher scores in the FND group relative to healthy controls (p = <.001).

6.4.2 Illness data

Data collected on illness duration indicated that the FND group (M = 9.99, SD = 74.08) did not significantly differ in illness duration in comparison to the LTD group (M = 13.91, SD = 9.16, t (866) = .278). However, the drastic difference between the variance of these scores should be noted. Data on diagnosis time was also collected for the FND and LTD groups. However, the dataset presented a challenge as illness durations were recorded in diverse units, ranging from years to hours. This posed a difficulty in cleaning and standardizing the data, which would have required a significant amount of time. Additional data on comorbidities in both groups would likewise require further clearing. Regrettably, given the constraints of time, it was decided that these analyses were not included to ensure the timely completion of the remaining research, which addresses the overarching thesis aims. Comorbidities were clearly seen in the FND group as 74.69% stated that they had other additional diagnoses. Triggers were analysed in relation to the Latent Class Analysis (Presented below).

6.4.3 Latent Class Analysis Subtypes

The LCA revealed seven distinct subgroups within the FND population, each characterised by unique symptom profiles and population shares. Class membership ranged from 6.62% to 22.71%, reflecting varying degrees of prevalence across subgroups. The maximum log-likelihood was -20008.69, with Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) values of 41093.38 and 43488.58, respectively.

Comparisons to alternative class solutions revealed that the 7-class model provided the best balance between model fit and complexity. While the 3 and 5-class solutions yielded the lowest BIC value, indicating a better fit, they failed to capture the full heterogeneity of symptom presentations observed in the data. Conversely, the 8-class, 9-class and 10-class solutions resulted in overfitting, as evidenced by negative degrees of freedom and higher AIC and BIC values. These higher-class solutions were negated due to increasing model complexity, which would remove class solutions from likely theoretical understandings. The 6-class solution offered a reasonable alternative, but the 7-class solution demonstrated superior model fit across multiple criteria, including maximum log-likelihood, AIC, BIC, and goodness-of-fit statistics. The 7-class structure showed a superior model fit characterised by a higher log-likelihood ratio (*LL* = -19949.55, *DF* = 96) and a lower Chi-Square goodness fit compared to other tested class structures, indicating better model fit. The Chi-Square Goodness of Fit (χ^2 (7) = 6.22, p = .08) was not significant, which, along with the entropy value (0.901), indicates good model fit with differences between the observed and expected data and good classification of accuracy meaning that the latent classes in the 7-class model are more distinct. Individuals are more clearly assigned to one class over another. A comparison of key model fit statistics can be seen in Figure 1.

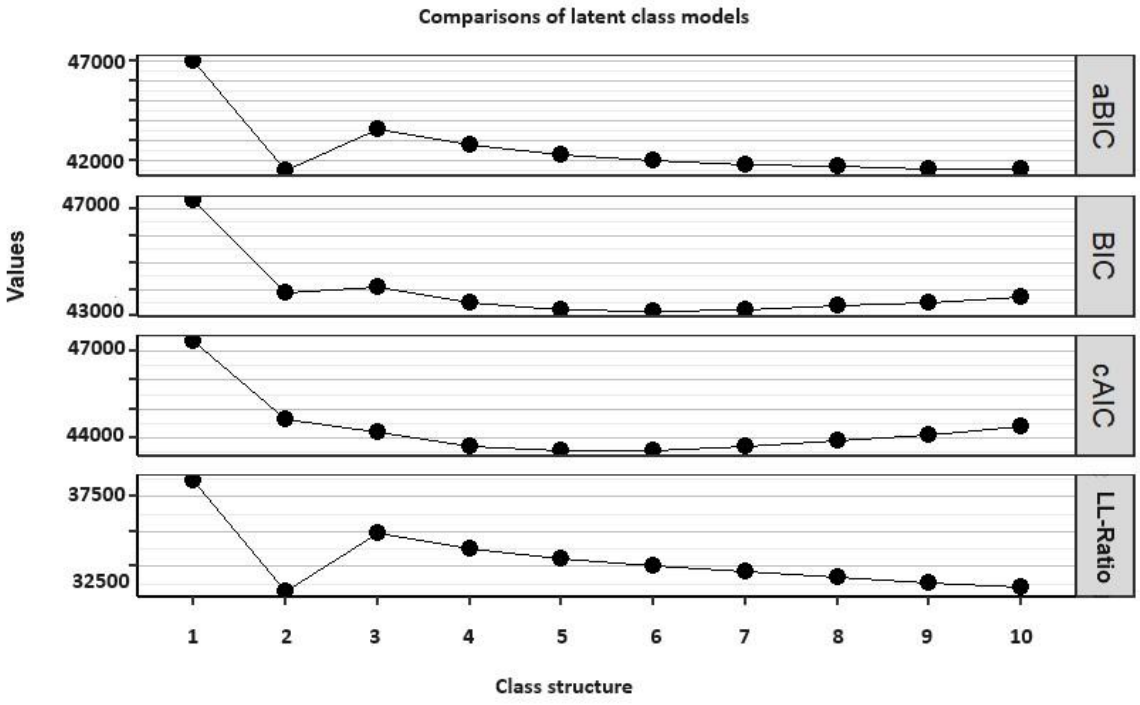

Figure 1: Comparisons of Fit Indices (aBIC, BIC, cAIC and Log-Likelihood Ratio) across latent class structures explored (1 – 10) in FND

Further exploration of the 7-class solution identified distinct subgroups within the data set, each characterised by a unique set of patterns and symptoms. Table 5 below provides a detailed description of each class within the identified 7-class structure and provides population estimates and predicted probabilities. Symptoms were explored using by examining by examining the conditional probabilities of symptoms and their relation to each class.

Table 6: Descriptions of the classes identified in the 7-class structure based on characteristics of symptom clusters (Study 2, Chapter 6)

Class No.	Assigned name	Est. Population share (%)	Pred Population share	Description
1	Motor Dissociation States	6.31%	0.0647	The smallest in terms of population share. Symptoms that appear all the time in this group are those associated with movement, including Walking difficulties (S1), one-sided heaviness (S2), Dissociated Limbs (S4), limb numbness (S5), Limb coordination (S6), and Paralysis (S7). Occasional symptoms of coordination issues (external; S3) and facial spasms (S15) were reported.
2	Non-Responsive Tremor	11.33%	0.1136	Core and often occurring symptoms in this class include Unresponsive States (S10), Staring and unable to respond (S11) and conscious convulsions/ tremors (S12). Of note all other symptoms (S1 – S7, S13 – S16, S19 – S38) could occur some of the time. The only symptoms that were not of probabilistic relevance to this class were Blackouts (S8), Seizures (S9), Tics (S17) and Jerks/Twitches (S18).
3	Polysymptomatic Seizure	21.39%	0.2129	This group identified core occurring symptoms related to impaired motor processes (S1 – S7) and Seizure subtypes (S10 – S13). Notably, all symptoms in this class were rated at least occurring some of the time, denoting a subclass with seizure and motor issues as well as regular other problematic symptoms.
4	Occasional Neuropathic	12.98%	0.1309	This group was only characterised by occasional occurrences of neuropathy (S3 coordination issues and S5 tingling and numbness). All other symptoms were rated at 0.
5	Mixed Multisystem symptoms	20.48%	0.1987	Many symptoms in this group related to motor processes but a large collection of symptoms was reported across this group as occurring some of the time.
6	Intermittent Seizure-Movement	14.58%	0.1498	Symptoms S1 – S3 and S5 (all related to movement issues) were rated as being present all of the time. This group also reported occasional probabilities of other motor difficulties and seizures. This subgroup is characteristic of seizures and movement difficulties which occur more sporadically.
7	Occasional Dystonic	12.93%	0.1293	This group reported occasional motor difficulties, particularly S1, S3, S5, S6 and S13, suggestive of Dystonic motor issues which occur sporadically. All other symptoms reported as 0.

Further exploration of symptoms highlights how these 7-class structures are characterised by both symptoms, which are present all the time, and potential occurrences some of the time. There is still great heterogeneity in the sample outline, demonstrating the chaotic nature of illness narratives and the mixed nature of likely symptom subgroups. There are, however, distinct differences within the classes; for example, whilst both class 3 and class 6 contain similar symptoms, which suggest dysfunction in both motor and seizures, class 3 probabilities suggest these are a more regular occurrence, whereas class 6 shows these symptoms more intermittently. Class 4, occasionally neuropathic, displays only two core symptoms, and further investigation of this, including correlates of the latent class, might help to appreciate this finding. This is distinctly different to the occasional dystonic subgroup (class 7), which demonstrates more fixed and dystonic movement issues. Class 1, Motor Dissociation, accounted for the smallest share but is synonymous with descriptions within the literature of Functional Movement Disorder. Of note in this class was the occurrence of dissociated and reduced movements. Whereas in Class 2, the Non-responsive Tremor was characterised by more excessive movements.

In Table 6, after outlining the characteristics of latent classes, further investigation was drawn to the likely probabilities associated with each symptom in each class. Figure 2 presents a visual representation of this data, illustrating the probabilities of each symptom in relation to each latent class. This figure clearly demonstrates the distribution of symptoms across latent classes but is indicative of the need to explore further class structures owing to mixed profiles.

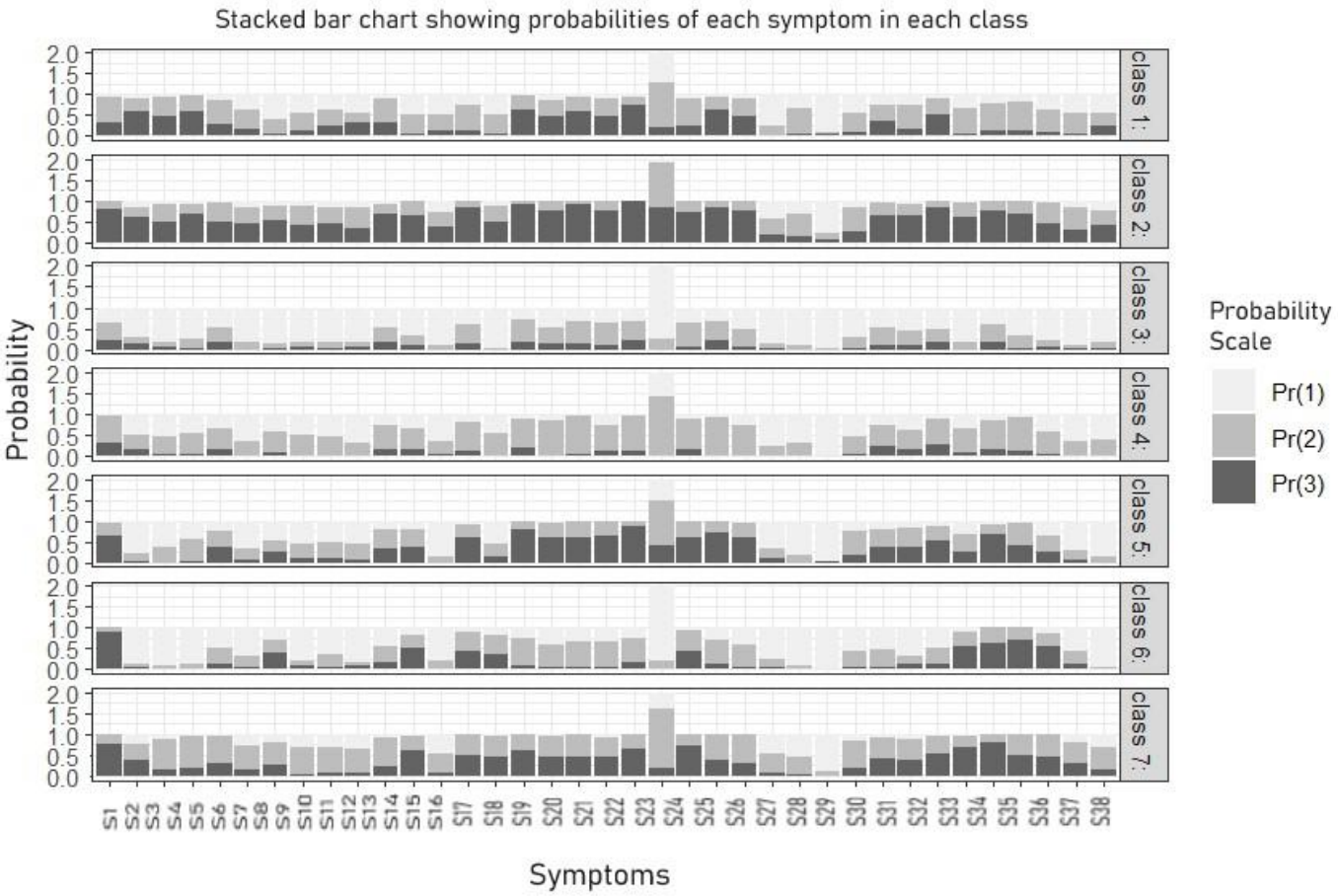

Figure 2: Probability of Symptoms (S1 – S38) in each identified latent class (1 – 7)

6.4.4 Latent Transition Analysis (LTA) of Additional Symptoms

LTA can be used as an expansion to LCA and was used to explore the transitional probabilities indicated with additional symptoms in relation to the identified symptom clusters of the LCA. LTA allowed for the modelling of changes to class membership and provided confirmation of a final latent class structure. The results revealed that there was a significant difference between the full and reduced models (x^2 (108) = 488.66, p <.001). This suggests that the additional symptom variables collectively and significantly affect class membership and should be considered as part of the core symptoms. This is further supported by model fit indices, which support the adequacy of the 7-class latent class structure even with consideration of the additional symptoms.

The logistic regression analysis explored the relationship between additional symptoms and class membership within the sample. Across the seven identified classes, varying patterns

of symptom influence emerged. Notably, Chronic Pain (A1), Persistent Fatigue (A2) and Insomnia (A3) demonstrated significant associations across multiple classes. For instance, in Class 2, Chronic Pain exhibited the strongest influence (β = 2.58), followed by Chronic Urinary Retention (β = 1.78) and Hearing issues (β = 2.15). Similarly, in Class 3, Persistent Fatigue (β = 1.91) and Insomnia (β = 1.23) emerged as the most influential symptoms, along with Hearing issues (β = 1.87).

Conversely, Class 7 displayed distinct associations, with Persistent Fatigue (β = -2.40), Dysfunctional breathing (β = -2.53), and Insomnia (β = -0.27) exerting notable effects. Whilst in Class 1, Hypersomnia (β = 0.43) and Migraines (β = 0.61) showed modest associations, while in Class 4, Hypersomnia (β = 1.25), Migraines (β = 1.19), and Anxiety and Panic Attacks (β = 1.59) emerged as significant predictors. Class 7 exhibited strong associations with Persistent Fatigue (β = -2.40), Dysfunctional Breathing (β = -2.53), and Insomnia (β = -0.27).

Further examination revealed class-specific symptom profiles, suggesting nuanced relationships between certain symptoms and class membership. For instance, in Class 6, Other headaches and facial pain (β = 2.40) and Dysfunctional Breathing (β = 2.07) emerged as primary influencers, whereas Class 5 demonstrated strong associations with Persistent Fatigue (β = 2.09), Hypersomnia (β = 2.32), and Anxiety and Panic Attacks (β = 1.94). These findings support the notion of additional symptom contributors to the identification of meaningful subgroups and are added to Table 7, along with findings of precipitating events for full descriptions of identified latent classes.

6.4.5 Relationships between Subtypes and Triggers

Owing to the categorical nature of variables, Likelihood ratio tests were used to assess the overall fit of the multinomial logistic regression model predicting latent class membership based on trigger (or precipitating) variables in those with FND. The results revealed a significant chi-square statistic (x^2 = 163.08, p <.001), indicating that the full model provided a significantly better fit to the data compared to a reduced model. This suggests that triggers contribute to the prediction of latent class membership.

Further examination of individual triggers and coefficients revealed significant contributions of a selection of triggers to class membership. Of note the triggers Viral Infection (x^2 = 19.31, p = .004), Head Injury (x^2 = 15.54, p = .008), Operation or Surgery (x^2 = 19.09,

p = .024) and No Triggers (x^2 = 20.71, p = .014) indicated significant contributions to model fit. The coefficients of each trigger were compared for each identified class and have been added to Table 7.

6.4.6 Relationships between Subtypes and Dissociation

Logistic regression analysis examined the association between class membership and total dissociation score. The analysis revealed a significant coefficient for Dissociation total (β = 0.018, *SE* = 0.009). The associated Z value of 2.076 and p-value of 0.03 suggest that dissociation scores influence the likelihood of class membership (as denoted by clusters of symptoms). The model's goodness-of-fit was assessed using the null deviance, residual deviance, and AIC. The null deviance, which represents the deviance when only the intercept is included in the model, was 392.62 (*df* = 423). The residual deviance, which measures the deviance when the predictors are included, was 387.91 and the AIC (Akaike Information Criterion) was 391.91.

Further analysis revealed that the probabilities of class membership could be noted based on levels of dissociation. Notably, high levels of dissociation were probabilistically more strongly associated with Class 1 (0.862), Class 4 (.8767), Class 5 (.8362) and Class 6 (.8150). Overall, the logistic regression model provides support for a significant relationship between total dissociation scores and class membership, with higher levels of dissociation associated with increased odds of certain class memberships. These relationships have been considered and added to Table 7 which provides a full description of all associations of each class.

Table 7: Latent Class Descriptions in relation to symptom clusters, additional symptoms, dissociation and predisposing (triggering) events

Class No.	Assigned name	Est. Population share (%)	Description	Additional Symptoms & Dissociation	Triggers Highest coefficients
1	Motor Dissociation States	6.31%	Symptoms that appear constantly in this group are those associated with movement, including Walking difficulties (S1), one-sided heaviness (S2), Dissociated Limbs (S4), limb numbness (S5), Limb coordination (S6), and Paralysis (S7). Occasional symptoms of coordination issues (external; S3) and facial spasms (S15) also occur.	Hypersomnia Migraines High dissociation	Head Injury Physical injury Viral Infection
2	Non-Responsive Tremor	11.33%	Core and often occurring symptoms include Unresponsive States (S10), Staring and unable to respond (S11) and conscious convulsions/ tremors (S12). Of note all other symptoms (S1 – S7, S13 – S16, S19 – S38) could occur some of the time. The only symptoms not of probabilistic relevance were Blackouts (S8), Seizures (S9), Tics (S17) and Jerks/Twitches (S18).	Chronic Pain Chronic Urinary Retention Hearing issues	Viral infection Operation/Surgery
3	Polysymptomatic Seizure	21.39%	Core occurring symptoms related to impaired motor processes (S1 – S7) and Seizure subtypes (S10 – S13). Notably, all symptoms in this class were rated as at least occurring some of the time, denoting a subclass with seizure and motor issues as well as other regular problematic symptoms.	Persistent Fatigue Insomnia Hearing issues	Head Injury Symptoms since childhood
4	Occasional Neuropathic	12.98%	This group was only characterised by occasional occurrences of neuropathy (S3 coordination issues and S5 tingling and numbness). All other symptoms were rated at 0.	Hypersomnia Migraines Anxiety High dissociation	Viral infection Head Injury Operation/Surgery No triggers
5	Mixed Multisystem symptoms	20.48%	Many symptoms in this group related to motor processes, but a large collection of symptoms was reported across this group as occurring occasionally.	Persistent Fatigue Insomnia High Dissociation	Viral infection No Triggers
6	Intermittent Seizure-Movement	14.58%	Symptoms S1 – S3 and S5 (all related to movement issues) were rated as being present all the time. This group also reported occasional probabilities of other motor difficulties and seizures. This subgroup is characteristic of seizures and movement difficulties that occur more sporadically.	Other headaches and facial pain Dysfunctional breathing High dissociation	Operation/Surgery Childbirth
7	Occasional Dystonic	12.93%	This group reported occasional motor difficulties, particularly S1, S3, S5, S6, and S13, which suggest sporadic Dystonic motor issues. All other symptoms were reported as 0.	Persistent Fatigue Dysfunctional Breathing Insomnia	Stress/burnout Trauma No Identified Triggers

6.5 Discussion

The present cross-sectional study aimed to explore the presence of subtypes of FND. First, a comparable study was conducted between those with FND, Healthy controls and an LTD population to add further insight into the results obtained in Chapter 5. Next, novel forms of statistical analysis for the field were applied, LCA and LTA analysis, to explore the potential presence of subtypes in FND. The research aimed to explore if subtypes exist which can be characterised by clusters of symptoms. The research then expanded upon this by the inclusion of an LTA as an extension of the LCA to explore additional other (non-core symptoms). Finally, the relationship between symptom clusters and the precipitating factor in FND was conducted, and explorations of other characteristics like dissociation were investigated to see if these differentially were associated with FND subtypes.

In relation to between-group findings, the work presented here further supports the notion that Anxiety, Depression and Stress are not specific to FND. Whilst significant differences were noted between the FND and Healthy Control group, this was also emulated by the findings of the LTD and healthy group. As no significant differences were noted between the LTD and FND groups, findings of higher anxiety, depression, and stress scores could be related to chronic illness in general rather than being specific to FND. This amplifies the need to conduct research which considers additional control groups, such as other illness controls, to avoid jumping to conclusions in this field (Pick et al., 2020). Several studies report a finding of high prevalence of mood disorders in FND (Akyüz et al., 2017; Butler et al., 2021; Pick et al., 2020; Perez et al., 2021; Şar et al., 2004). However, these do not always consider associations with other illness groups. Whilst co-occurring symptoms worsen clinical outcomes and are as disabling as the core features of FND (Gelauff et al., 2014; Glass et al., 2018; Nicholson et al., 2020) and worsen quality of life (LaFrance et al., 2009; Jones et al., 2016) mood disorders may reflect something beyond this. However, not all research has demonstrated a link between FND and co-occurring disorders of mood, with some finding low rates in FND cohorts (Fobian & Elliott, 2019; van der Hoeven et al., 2015). It should also be acknowledged that other neurological disorders (e.g., Multiple Sclerosis, Epilepsy, Fibromyalgia and Parkinson's) are also associated with high levels of anxiety, depression and dissociation (Bulloch et al., 2015; Davies et al., 2001; Karatzias et al., 2017). This is further supported by the findings of the current study, which found no differences between scores of those with other long-term conditions and FND.

Between-group differences were also noted for cognitive flexibility, burnout and quality of life. Quality of life has been noted as being lower in FND in previous research (Butler et al., 2021; Gendre et al., 2019; Jones et al., 2016). Results presented here indicate that those with FND have a significantly lower quality of life compared to both healthy controls and those with other long-term conditions. This signifies that Quality of life is not merely a product of chronic illness but is likely influenced by other factors in FND, perhaps including stigma, reduced health care provisions and chaotic illness narratives. Findings of reduced cognitive flexibility may also indicate a more fixed mindset in those with FND, which could influence treatment outcomes and should be carefully considered in investigations of symptom characterisation and as a biological outcome (Alluri et al., 2020; Graham et al. 2018). Personal burnout was notably higher in FND. Whilst this has previously been considered as a factor which may contribute toward the onset of FND, here it is noted that this score is high post-diagnosis. Careful consideration should be given to the meaning of this finding, and further exploration as to why burnout is higher should be noted, as this, too, seemed more prevalent within the FND than the long-term illness group.

Again, the results here support those of Chapter 5 and of previous research (e.g. Blanco et al., 2023; Campbell et al., 2023; Pick et al., 2020) and support the notion that elevated dissociation in FND is prevalent relative to both healthy controls and those with other long-term illness across most dissociation subscales. Elevated dissociation may be particularly prominent in FND and pose a significant additional difficulty for those with FND (Holmes et al., 2005; Pick et al., 2017). Given the high variability of dissociation in the FND group, it is possible that dissociation may be particularly associated with certain subtypes, such as Functional Seizures (Goldstein & Mellers, 2006); Functional Seizure subtypes are also associated with raised dissociation compared to those with epilepsy (Myers et al., 2019). The identification of such FND subtypes, characterised by dissociation, might have implications for tailoring treatment for FND. Dissociation was associated with higher disability scores and could reflect generally higher disability and impairment to quality of life than those with other organic disorders (Carson et al., 2011).

The identification of seven distinct latent classes, based on cluster analysis of 38 core FND symptoms, suggested a nuanced understanding of the underlying potential FND subgroups. Whilst current diagnostic criteria allude to a multitude of experiences and symptoms in FND, this creates further conceptual confusion (Ball et al., 2020; Hallet et al., 2022). The findings from this exploratory LCA support that there could be at least seven

subclasses of FND. In doing so, the data provides support for those who call for the exploration of different phenotypes of FND (Hallett et al., 2022; Fiorio et al., 2022; Stone et al., 2004;). Whilst the data could not capture clinical observations of those who present with more than one phenotype or who alternate between phenotypes, it does provide a starting point for these discussions. Of note, further considerations should be given in the refinement of the scale to capture subtle symptom nuances (such as distinguishing between different types of seizure) and in capturing so-called Functional Cognitive Disorder (Ball et al., 2020). The findings so support the notion that functional seizure subtypes may have difficulty in motor states in addition to seizure symptoms, but large heterogeneity in some of the mixed groups warrants further explorations.

Additional explorations of the latent classes identified revealed a significant contribution of 'additional' symptoms, i.e., symptoms like chronic pain and fatigue which are often assumed to be a part of an FND diagnosis but not specific to FND (Butler et al., 2021; Teodoro et al., 2018). These played a significant contribution to the model and posted strong associations across most of the 7 subtypes, indicating that these could be considered as part of the core symptoms, particularly if these have a role in differentiating between subtypes of FND. These symptoms are noted as having clinical significance (Kranick et al., 2011; Nicholson et al., 2020; Popkirov et al., 2019; Stone et al., 2010), negatively influence clinical outcomes (Gelauff et al., 2014; Glass et al., 2018) and are often just as disabling as the core symptoms noted (Glauff et al., 2018). Thus, the current research supports the notion that these should be included as core symptoms in the development of symptom profiles and in further explorations of this area.

The current study also explored precipitating factors and dissociation in relation to the seven identified classes or subgroups of FND. Previous research has noted that precipitating factors are common and commonly have a relationship with the type of symptoms experienced (Geroin et al., 2022; Butler et al., 2021; Geflauff et al., 2019; Forejtova et al., 2021). The current research suggests that some precipitating factors (particularly viral infection, head injury and operation and surgery) may be influential in the development of specific subtypes of FND. However, a notable proportion of participants did not identify any clear precipitating event preceding their symptom onset. The absence of a discernible trigger was strongly associated with several of the identified symptom clusters, raising important questions about alternative mechanisms driving symptom onset in these cases. While FND has historically been linked to psychological or physical precipitating events, research increasingly recognises that not all

individuals with FND report identifiable triggers (Ludwig et al., 2018; Perez et al., 2021). This finding aligns with contemporary perspectives suggesting that FND can emerge through multiple pathways, some of which may involve insidious onset, predisposing neurobiological vulnerabilities, or cumulative stressors rather than discrete triggering events (van der Feltz-Cornelis et al., 2020). Given the heterogenous nature of FND, the results suggest that symptom clusters may not always develop in direct response to a single identifiable event but could instead arise from long-term neurobiological dysregulation, a culmination of biopsychosocial factors or in some cases, that allostatic load may be pinpointed to a singular event. Further investigation is needed to validate these symptom clusters and explore how different FND subtypes may relate to distinct underlying mechanisms. Additionally, dissociation scores were strongly associated with some of the latent classes identified, reinforcing their role as a potentially differentiating factor in FND subtypes. Future work should continue to explore the relationship between dissociation and symptom clusters, as this may have significant implications for treatment stratification and clinical outcomes. Notably, further research could be undertaken to validate symptom clusters and their relationship to different types of dissociation.

In the realm of psychological phenomena, LCA serves as a valuable tool for discerning underlying structures amidst seemingly disparate manifestations, and here, it has been extended to FND. By employing LCA, there has been an exploratory and successful attempt to discern distinct subgroups within the heterogeneous FND population, shedding light on potential clusters of symptoms and their interrelations (Stone et al., 2020). These findings resonate with the tenets of chaos theory, which posits that complex systems, like FND, are sensitive to initial conditions, wherein small variations can lead to vastly different outcomes (Gleick, 1987). In this context, the identification of symptom clusters through LCA mirrors the intricate dynamics of deterministic chaos, where seemingly minor differences in symptomatology can precipitate significant variations in the progression and manifestation of FND (Jones & Stone, 2021).

Moreover, extending the analysis to explore correlations with precipitating events, dissociation, and additional symptoms adds another layer of complexity reminiscent of chaos theory. Just as chaos theory emphasises the notion of the butterfly effect, where small changes in initial conditions can lead to large-scale effects (Lorenz, 1963), the exploration of these correlations within the context of FND underscores the nonlinear and interconnected nature of the disorder. For instance, the identification of specific precipitating events or the presence of dissociative experiences may act as catalysts, triggering cascading effects throughout the

symptomatology of FND. Such observations underscore the intricate and dynamic interplay between various factors within FND, highlighting the need for comprehensive and nuanced approaches to researching, understanding and treating the disorder. Chaos theory notions to explorations of FND also support an understanding of these dynamics and offer promising avenues for the advancement of theoretical frameworks.

This study is not without its limitations. Whilst a data-driven cluster analysis technique was employed here to provide a data-driven approach to FND Subtypes with LCA analysis in an unbiased fashion, this is an emerging investigation tool. Across illness groups, other studies have failed to identify clusters, including in Parkinson's disease (Ba et al., 2016; Mu et al., 2017; Starkstein et al., 2011) and fibromyalgia (Sullivan et al., 2002; Schmalbach et al., 2021; Yim et al., 2017). As with these studies, there is a potential for false-positive cluster identification. One potential limitation of latent class analysis is that the number of classes is sometimes equivocal, analogous to the difficulties often encountered in determining the number of factors to interpret in factor analysis. Thus, inferences about the specificity of the current findings are not entirely possible, and further studies are needed. Indeed, this is particularly important in the absence of a validated scale of FND. Whilst this study provides support for the notion of different subtypes of FND, to ensure robustness further research needs to consider the validity of the symptom list and incorporate additional symptoms. This needs to be explored before neurobiological research can investigate potential nuances in the underlying mechanisms underpinning each subtype.

The patterns observed within each class offer insights into the heterogeneity of symptom presentations and clusters of such presentations. These findings highlight the presence of heterogeneity in FND symptomatology, suggesting underlying differences in aetiology, pathophysiology, and clinical manifestations. Further investigation into the symptom profiles of each class is warranted to elucidate their unique characteristics and inform personalised treatment approaches. Understanding the distinct subtypes of FND can facilitate targeted interventions, optimise clinical care, and enhance outcomes for individuals with this complex disorder. Additional explorations of precipitating factors, additional symptoms, and dissociation offer further insight into this area.

6.6 Chapter Summary

This chapter has further explored the role of dissociation in relation to differences between control groups (healthy and other long-term conditions) and in relation to other correlates of FND such as quality of life, burnout and cognitive flexibility. Whilst a latent class structure and seven potential FND groups were identified within this work, this is a very early-stage exploratory study, and much more work is needed to validate these subtypes before neurobiological evidence is conducted on these subtypes. Thus, the chapters to follow explore neurobiological explorations of FND in the absence of these proposed subtypes. Chapter 7 considers the relationship between inflammation, dissociation and brain activity in FND.

Chapter 7: Inflammation, Dissociation and Brain Function in FND

7.1 Chapter Introduction

Previous chapters have explored FND and identified dissociation as a core feature within this (Chapter 5) and prevalent across a range of symptom clusters in FND (Chapter 6). The current chapter, therefore, advances on these ideas and proposes that FND is a condition of the embodied brain in which there is a relationship between physiological and homeostatic functions, brain activity (or dysfunction) and psychological correlates such as dissociation. The current chapter proposes that a mediating factor that has been less studied in FND and which accounts for these mechanistic underpinnings of the disorder is inflammation. The chapter presents a multimodal exploratory study which aims to understand the role of inflammation in FND and its relationship to brain activity (measured by baseline resting state data) and dissociation. Further considerations were given to electrode clusters which represent distinct areas of interest in FND and their relationship to inflammation and dissociation.

7.2 Introduction

As this thesis has demonstrated, FND is a complex disorder involving many disturbances of bodily function. It is likely that there are symptom clusters that could explain some of the heterogeneity of FND symptoms (as outlined in Chapter 6). Despite this, many believe that a common mechanism operates beneath all FND subtypes, yet research has yet to establish what this mechanism is. A way to view FND is as a condition which defies dualism and a disorder which goes beyond theories of neural network dysfunction and includes the conceptualisation of FND as a disorder of the embodied brain (one in which there is dysfunction in neural networks as well as bodily systems and psychopathology). Such a theory could also explain the accumulating data that suggests that there are fluctuations in the severity of symptoms and account for why some experience ‘attacks’ of symptoms rather than a simple presence or absence of symptoms (McEwen et al., 2015). An underlying mechanism which has, to date, received very little attention in FND is that of the inflammatory system. It is this that the current study sets out to explore as a potential underlying mechanism in FND.

It is widely acknowledged that a complex network involving bidirectional signals is constantly exchanged between the nervous system, neural networks, and endocrine and immune systems, which can influence cognition, mood and wider functioning (Maier, 2003). For instance, research into chronic stress underscores how persistent activation of the HPA and ANS leads to inductive changes in the immune system through the release of hormones (Glaser & Kiecolt-Glaser, 2005). Chronic activation of inflammatory pathways can also modify the synthesis of neurotransmitters, heighten stress responsiveness and impact cognitive domains, such as learning, memory and executive function (Kiecolt-Glaser et al., 2015; Švob et al., 2016). Inflammation itself is a complex biological response, but chronic inflammation is known to result in tissue damage and contribute to neuroinflammation wherein chronic states, which fail to return to manageable levels, affect nervous system function (Castellheim et al., 2009; Nathan & Ding, 2010). Neuroinflammation has been acknowledged as a component in the pathogenesis of nervous system conditions including neuropathic chronic pain (Kim et al., 2007; Martini & Wilson, 2016; Myers et al., 2006) and diseases of the central nervous system, including mood disorders (Calsolaro & Edison, 2016; Castanon et al., 2015; Najjar et al., 2013; Wohleb et al., 2016) and autism (Thoharides et al., 2016). Despite this, very little literature has delved into the potential pathogenesis of FND as influenced by neuroinflammation.

Whilst several mechanisms are proposed by models of FND, its specific origins remain unknown (Ratcliffe & van der Feltz-Cornelis, 2020). A plausible explanation more recently being considered is systemic low-grade inflammation or neuroinflammation (Del Grande da Silva et al., 2016; Kovacs et al., 2016). To date, research has found elevated CRP in children with FND (Kozlowska et al., 2019) and in adults with FND who have motor function difficulties over other subtypes or symptom profiles (Tak et al., 2009). Owing to the reciprocal bidirectional nature of corticosteroid influences, this could result in peripheral inflammation, which could not be easily reversed and could account for the symptoms seen in FND (Pongratz & Straub, 2014). However, CRP as a measure is somewhat generic and can be highly sensitive and inflammatory processes can be studied more specifically.

The inflammatory response is adaptive and lends to disrupted homeostasis mediated through the production of various cytokines (Becher et al., 2017; Dantzer et al., 2008), including commonly studied proinflammatory cytokines (the interleukins, e.g. IL-1β, IL-2, IL-6 and TNFα). High concentrations of pro-inflammatory cytokines in response to infection are adaptive responses which contribute to survival during infection (Dantzer et al., 2008) and could account for so-called “somatoform” symptoms seen in FND including drowsiness,

fatigue, cognitive fog or 'fugue', joint pain, dissociation and reduced social activity. In FND, neuroinflammation is beginning to be recognised across several cytokines. For example, Van der Feltz-Cornelis et al. (2021) found elevated levels of IL-6 and TNF-alpha in FND using a relatively small cohort (n = 14). Fluctuations of these cytokines may affect physiological processing, including the formation and organisation of neural networks, and influence cognitive function effectiveness (Dantzer & Kelly, 2007; Levin et al., 2021). Fluctuations may also account for slump-crash reactions in FND and co-ordination of cells throughout the body; thus resulting in dysfunction in many functions, such as thermoregulation, eating, sleep, emotion, cognition, learning, memory and others through modulation of synaptic transmission and neuroplasticity (Becher et al., 2017; Levin & Godukhin, 2017; McAfoose & Baune, 2009; McKim et al., 2016; Osipova et al., 2018).

These findings do not sit in isolation from other research findings in FND. For example, research exploring brain function in FND suggests that arousal and emotion-processing regions are overactive and dominant in those with FND, showing hyperconnectivity with motor regions, which in turn disrupts motor regions, leading to symptoms of motor dysfunction (as reviewed in Blakemore, 2016). Emotion-processing dysfunction in FND has also been attributed to increases and decreases in grey matter in both motor and emotional processing regions in adult patients with FND (Atmaca et al., 2006; Aybek et al., 2014; Labate et al., 2012; Nicholson et al., 2014; Perez et al., 2017). Psychological correlates of inflammation should be induced through allostatic load (as reviewed in Chapter 3, Section 3.5.3). The allostatic load was recently measured by an index of 11 biomarkers of metabolic, cardiovascular, inflammatory and HPA and ANS activity and particularly implicated high levels of IL-6, CRP and lower cortisol, which could support this model of inquiry in FND (Keynejad et al., 2019). In exploring the psychological correlates of FND, a study exploring the cortisol awakening response using salivatory cortisol showed that dysregulation of this in FND correlated with ALEs (particularly childhood adverse experiences) and subjective distress (Chung et al., 2023). The findings, however, also support the idea that neural underpinnings of FND may extend across arousal-processing and emotional-processing systems. Despite these findings, dissociation has yet to be studied in relation to inflammatory markers in FND. Nevertheless, in other disorders, dissociation has been associated with inflammatory processes (e.g., Grassi-Oliveira et al., 2008; Lamb et al., 2021; Staniloiu et al., 2010).

Similarly, the brain's innate immune effector cells, glial cells, confer immunological memory and these play an important role in neuroplasticity (Frank et al., 2016; Ji et al., 2016;

von Bernhardi et al., 2016) and could play a role in the experience-dependent plasticity changes seen in those with FND (Kozlowska et al., 2018; Stephenson & Baguley, 2018). Further, an inflammatory exploration of FND may enable the progression of understanding of the cognitive dysfunction seen in those with FND. A range of neurocognitive issues, including motor cognition and information processing speed and accuracy, occur in FND (Baumeister et al., 2016; De Vroege et al., 2020), which could be indicative of neuroinflammation affecting brain activity and neurocognitive function. Particularly, research has postulated dysregulation of the HPA axis in those with FND, but its relationship to anatomical and biological states remains to be elucidated. Weber et al.'s (2024) study explored the HPA in relation to inflammation by utilising cortisol awakening responses and diurnal baseline cortisol in 86 patients with mixed FND symptom profiles. HPA dysregulation and changes in glucocorticoid signalling on a molecular level may contribute to increased vulnerability to FND because of epigenetically mediated changes to the neural networks implicated (Chung et al., 2023). However, these changes could also result from the biological insult posed by FND, and changes could reflect effect rather than causality. Whilst an important and notable finding, this again does not consider more stable trait markers of inflammation, including IL-6 and CRP, which are recognised as key markers of systemic inflammation (Gabay & Kushner, 1999; McInnes & Schett, 2017; Ridker et al., 2000; Povoa et al., 2005). This is an important area to address, not only in advancing theory, but also given that these neurocognitive symptoms have been found to strongly influence treatment effectiveness and illness progression (De Vroege et al., 2017).

Whilst previous research in FND has relied upon task-based research, to progress understanding of FND, it is also important to look at resting-state data. As reviewed throughout Chapter 3, resting state data analysis, particularly that of electrophysiological data, has been under-utilised as a research tool within the field of FND. Contemporary imaging studies have enabled the identification of functional networks which are central to the organisation and function of the brain during both rest and task-based states (Raichle, 2015; Williams, 2017).

The Default Mode Network (DMN) is a group of nodes located in the medial prefrontal cortex, posterior cingulate and precuneus cortex, and lateral temporoparietal cortex. Its primary function is to facilitate self-directed thinking and the ability to transition between alert states (Hagmann et al., 2008; Raichle, 2015). Mental health disorders have been linked to specific dysfunctions within the DMN (Williams et al., 2017; Wang et al., 2016), and it is possible that dissociative disorders, including FND, may also involve disruptions within the DMN.

In addition to the DMN, the salience network, which consists of the limbic network defined by the anterior insula, dorsal anterior cingulate cortex (ACC), and amygdala, plays a role in energy regulation. According to Kleckner et al. (2017), the DMN and salience networks work together as a single, allostatic-interoceptive brain system that regulates energy and supports various psychological functions, such as emotion processing, pain processing, memory, and decision-making. This brain system predicts the body's energy needs and regulates the body's physiological systems to maintain energy balance (allostasis). In response to danger, the system anticipates the body's increased energy needs and activates brain-body systems that support increased energy consumption. When the danger has passed, the system readjusts the energy-regulation system. However, continued activation of the system may increase the risk of stress-related physical and psychological disorders. Individuals with functional neurological disorders (FND) exhibit activation of the hypothalamic-pituitary-adrenal (HPA) axis, autonomic nervous system, and brain systems responsible for arousal and energy consumption. Kozlowska et al., (2018) showed that in children with FND there were distinct neural changes within the DMN. This suggests that maladaptive activation of the allostatic-interoceptive brain system, along with disruptions in motor systems, could be a core feature of FND, but has yet to be explored within adult populations and across mixed subtypes. Advancements in understanding in these areas, require multi-study investigations which consider the role of inflammation, dissociation and relationships with brain function.

7.2.3 Aims and Hypotheses

Research in this area shows great promise for progressing the understanding of FND and leading to more holistic treatment methods. However, there are several limitations of previous research to note. Firstly, an overreliance on cortisol limits understanding of chronic inflammatory states. Cortisol can be influenced by various factors beyond inflammation, including stress, medications and circadian rhythm, and its lack of specificity and diurnal fluctuations somewhat limit its reliability as a sole biomarker of inflammation (Chrousos, 1995). Thus, an important consideration in advancing research in this area is the exploration of wider, more stable markers of systemic inflammation. Secondly lack of inclusion of combined biochemical and brain activity data for robust multimodal designs. Studies in FND have yet to integrate molecular and neuroimaging for a holistic understanding of cytokine modulation in FND. Finally, whilst some studies have likened findings to stress responses and made

comparisons between ALEs and inflammatory levels in FND, there is a lack of consideration of further key biopsychological correlates which are important in the exploration of FND, such as dissociation. As such, the current chapter presents a multimodal experiment which explores inflammatory molecules in FND, alongside data on dissociation and brain function and, in comparison, to a healthy, matched control sample. Specifically, this multimodal exploratory study aims to address the following questions: 1) Are there differences in inflammatory markers (IL-6 and CRP) in FND compared to healthy, matched controls? 2) Are these differences maintained when mediations are considered for anxiety, depression, stress, BMI and dietary inflammation? 3) Do inflammatory markers correlate with dissociation, and are these different in FND compared to healthy controls? 4) Do baseline EEG measures correlate with inflammatory markers in FND?

Based on existing literature and theoretical frameworks, the following hypotheses are proposed:

- H1: Individuals with FND will exhibit higher levels of inflammatory markers (IL-6 and CRP) than healthy, matched controls.
- H2: Differences in inflammatory markers will persist after controlling for potential confounders such as anxiety, depression, stress, BMI, and dietary inflammation.
- H3: Higher dissociation scores will be associated with increased inflammatory markers, and this relationship will be stronger in the FND group than in healthy controls.
- H4: Individuals with FND will exhibit altered resting-state EEG activity at midline sites (including frontal, central, and parietal electrodes), as well as in key nodes of the Default Mode Network (DMN). These differences will be characterised by changes in oscillatory power and connectivity patterns compared to healthy controls.
- H5: Baseline EEG measures will show significant correlations with inflammatory markers in FND, suggesting an interaction between neurophysiological activity and immune function.

7.3 Methods

7.3.1 Participants

A sample of participants who had completed Study 2 (Chapter 6) were invited to reply via email to take part in this phase of the study. A sample of N = 78 took part in this experimental study, aged between 18 – 67 (*MeanAge* = 39.97, *SD* = 12.05, 62 females). This sample included 29 Healthy Controls (*MeanAge* = 39.38, SD = 14.18, 22 females, 7 males) and 49 people with a diagnosis of FND (*MeanAge* = 40.33, SD = 12.48, 40 females, 9 males). A matched design was ensured based on gender, age, lifestyle and handedness. Often, carers, partners, relatives, or friends of the patient group would act as healthy controls. There was no statistical difference in the mean ages of the groups (t (76) = .366, p = .759). Additional health factors were screened for during the recruitment process, particularly anything which may influence biological markers such as health conditions in both groups, pregnancy and lactation, recreational drug use, heavy drinking, smoking, heart conditions, diabetes, asthma and blood-thinning medications. Demographic and health data was also collected from the sample, which could influence biological markers but could not be fully controlled, including menstruation cycle, sedentariness in the last week, medications, height and weight and dietary intake within the previous two weeks. BMI was calculated, and the mean BMI of the FND group (M = 30.61, *SD* = 6.36) was significantly higher than the BMI of the Healthy Control Group (M = 25.88, *SD* = 25.88, *SD* = 4.89; f (1, 67) = 5.067, p = .028). This was further reflected by measures of sedentary activity suggesting that those in the FND group had more restricted and sedentary lifestyles compared to controls. FND patients also had a list of additional medications (in some cases rather large lists) which could not be screened out, and this, along with BMI, is considered in the analyses that follow.

7.3.2 Procedure

Participants were invited to participate in the online study and asked to indicate preferences to be contacted regarding this experimental phase of the study. Before coming in for assessments, participants completed online screening information which ensured that ethical and safe practices were applied and that there were no contraindicators to testing, particularly for phlebotomy measures. Participants were asked to fast for 12 hours prior to their

appointment, but to hydrate well (with water only) and to continue taking any prescribed medication as needed. Upon arrival at the lab, participants were greeted, offered water to ensure sufficient hydration and completed further screening and health questions. Participants were then weighed and had their height recorded. Participants were first invited to provide a blood sample (10ml of Venus blood was extracted). After ensuring participants' safety and supplying them with a healthy snack, participants participated in an EEG. The EEG consisted of 6 minutes of recorded data in total (3 minutes eyes open and 3 minutes eyes closed), and these conditions were randomly ordered to reduce the effects of fatigue and order effects. Upon completion, participants were debriefed and thanked for their participation.

7.3.3 Data collection & and processing

7.3.3.1 Psychological Markers Collection and Processing

To measure dissociation as a multi-construct model over a unitary model, Brière, Weathers, and Runtz's (2005) Multiscale Dissociation Inventory (MDI) was used. This assesses dissociation across 6 subscales to emulate contemporary notions of the multifaceted nature of dissociative experiences: Disengagement, Identity, Emotional, Memory, Depersonalisation and Derealisation. This scale veiled useful findings in the previous empirical studies (Chapter 5 and Chapter 6). The 30-item scale also generates a total dissociation score. The scale showed good psychometric properties and good internal validity (Cronbach's alpha = .96). The current study only employed the sum of the total dissociation score rather than exploration of the component parts as an initial exploration into the links between dissociation, inflammation and brain function.

Mood was measured using the *Depression, Anxiety and Stress Scale* (DASS-21; Lovibond & Lovibond, 1995) is a 21-item scale (7 items each for depression, anxiety and stress). Scores on each of the subscales ranged from 0 (none) to 3 (usually/always). The scale assesses dysphoric mood states including self-depreciation, lack of interest, hopelessness, arousal states and emotional liability to stressors across the subscales. Only the Anxiety and Stress subscales were used in the present study. Summed scores were generated and multiplied by two to match the authors' recommendations. The scale has good psychometric properties (Cronbach's alpha = 0.80).

7.3.3.2 Other demographic and health status information

Demographics and health status were obtained in an online questionnaire before attending the lab on the day of testing. This online survey included the above psychological constructs: Dissociation, Depression, Stress, and Anxiety and asked for additional details, including age, handedness, sex and other markers, which could be used to assess overall health status to ensure a suitably matched design. Additional questions ensured rigorous screening to ensure that there would be no adverse effects to testing. This included screening for anyone with pregnancy, diabetes, heart conditions, and asthma, as these could influence levels of inflammation or act as adverse conditions, causing potential issues for testing. Upon attendance at the lab, participants were asked to complete further health status data, including providing lists of medications, additional conditions, information on menstrual cycle and activity level and stating any prior issues with blood samples. Participants were weighed on a set of standard metric scales, and height was obtained to calculate accurate BMIs.

7.3.3.3 Phlebotomy Collection and Processing

Prior to data collection, participants were required to fast for a minimum of 12 hours, consuming only water prior to their appointment to ensure that inflammatory data was not subsumed by dietary intake (as per literature recommendations, e.g., Langsted et al., 2014). IL-6 and CRP were selected as these are two of the most commonly assayed biomarkers of chronic, low-grade inflammation (e.g., Baumeister et al., 2016; Fagundes & Way, 2014). Though of course, the role of these molecules extends beyond inflammation, they are a good starting point for exploratory studies as these molecules are easier to detect (Del Giudice & Gangestad, 2018). Venous blood was collected into an EDTA vacutainer (10ml), inverted to mix and stored in a fridge prior to processing. Each sample was centrifuged for 15 minutes at 1000 x g at 4°C within 30 minutes of collection. Plasma was decanted and aliquoted to 200uL cryotubes before being stored in a -80°C freezer until analysis. Processing of samples followed approved guidelines.

Uncoated multiplex ELISA plates from MESO Scale Discovery (MSD, Gaithersburg, USA) were selected for assays as they allow for sensitivity at low concentrations as well as the high dynamic range of standard curves and inter-plate low reliability. Panels were coated according to ELISA processes with minimal modifications to ensure maximum optimisation and accuracy. All plasma samples from healthy controls and patients were assayed in duplicate

immediately after the first thaw. Repeated freeze/thaw cycles were avoided to ensure sample preservation and to avoid degrading sample proteins. Once plates were coated, 50 µl of each diluted sample was added to the well of the 40-well plate and incubated at room temperature for 2.5 hours. The plates were then washed three times with a Wash Buffer (MSD) and Sulfotag Detection Antibody (MSD). Finally, plates were washed again and 150 µl of read buffer was added prior to being scanned by a SECTOR Imager 6000 Reader (MSD). IL-6 levels are reported as a mean after the mean zero standard has been subtracted.

7.3.3.4 Electroencephalography Recording and Processing

Each participant's resting state EEG data were recorded for 3 minutes per condition (eyes open and eyes closed). EEG was recorded with a NeuroScan Nuamps Amplifier (Compumedics, USA) based on an extended 10-20 placement via 34 Ag-AgCI electrodes which were mounted onto a Quik-Cap. The reference electrode was Cz and the ground electrode was located at a frontopolar midline position. Measurements were taken of participants' heads in line with standard EEG collection convention, to ensure correct fitment and placement and position of the cap in each instance. Additional electrooculogram (EOG) electrodes were placed at the outer canthus of each eye, and vertical EOG electrodes were placed above and below the right eye. Impedance was maintained at below 5 kΩ throughout the recording and recordings were conducted with a 1000-Hz sampling rate.

Signal processing was performed using CURRY 7.12 (Compumedics, USA). Data was initially refenced to a linked mastoid. Filters included a low-pass filter of 49Hz, high-pass filter of 1Hz and notch filter of 50Hz. Artefacts were reduced in the following way. Firstly, a semi-automated procedure identified noise in posterior channels and marked the area as a bad block. Data in the bad block were “flatlined”. Eye movement artefacts were then reduced. Frontal electrode channels were used to identify blink artefacts, and principal components analysis was used to extract blink-related activity from the data. Data files were then saved and reopened. EEG data was divided into 2s back-to-back epochs. Epochs with any further artefacts were removed, with the criteria that a minimum of 60 epochs were retained for each participant (equating to 2 minutes of clean data). During data processing, some samples were excluded from the analysis. Of the original 49 FND participants, 2 had adverse experiences in testing, which limited accuracy and noise in the recorded EEGs and 3 presented with abnormally high-frequency data. Of the original 29 controls, 3 declined to provide EEG and a further 2 were

excluded in data cleaning owing to excessive noise in the recorded data. A total of 44 FND participants and 24 Healthy Controls were retained for analysis.

Spectral analysis explored Delta (1 – 4 Hz), Theta 4-8Hz), Alpha (8-12Hz), Beta (12-30) and lower Gamma (30 – 49 Hz). Alterations in these frequency bands have been implicated in various neurological and psychological disorders, including those characterised by dissociative symptoms or inflammation (Clarke et al., 2001; D'Alessandro et al., 2003). Whilst whole brain analysis was reported across the scale, specific electrode clusters were also explored, which represent distinct brain regions and functional networks. This approach allowed for a more focused investigation of neural activity within regions of interest and aligned findings with stronger theoretical frameworks and previous research. Selective analysis of electrode clusters also enabled exploration of more meaningful relationships between neural activity and additional variables (Giacometti et al., 2014; Keil et al., 2014; Lemieix et al., 2001; e.g., dissociation and inflammation). Initial analysis and figures were based on frequency bands at frontal, frontal central, central parietal, temporal and occipital sites. Explorations then went beyond this to explore specific cluster sites of interest to the current research.

EEG power data were next quantified for specific regions of interest, particularly those which define the default mode network, salience and supplementary motor area networks. Channel selection was based upon the topographical map developed by Giacometti et al., (2014). Topographic mapping techniques were implied to infer underlying brain activity from scalp EEG data, though the inherent limitations in precise localisation of such an approach are acknowledged. Clusters of electrodes corresponding to regions of interest were identified and based on established literature (Giacometti et al., 2014; Kozlowska et al., 2018) facilitating investigation into neural correlates of dissociation and inflammation in FND. Channels selected for electrode clusters have been reported here to conform to best practices and the need for transparency in EEG studies (Keil et al., 2014). Due to the complexity and scale of the data set and conceptual disagreements within the literature, two further rounds of electrode clusters were explored. In particular, electrode clusters employed in previous EEG studies in children with FND were considered in this analysis (Kozlowska et al., 2018) to ensure that results could be interpreted with clear reference to work which has previously been done. In set 1, areas implicated in the DMN were explored as a whole including regions of the Medial and Posterior Cortex (mPFC, Electrodes CP4, CPz, Fp1, FT7, FT8, O1, O2, Oz, Pz) and Temporal and Parietal Regions were explored as a separate cluster (Electrodes F10, F9, P3, P4, P7, P8, PO1, PO2, T7, T8, TP7, TP8). The salience network was defined according to two core regions of

the network, the insula cluster and the dorsal ACC cluster (as per literature recommendations e.g., Seeley et al., 2007; Williams, 2017; Electrodes: F7, F8, Fz, F4). The Supplementary motor area, or SMA, was identified using further literature recommendations (Williams, 2017) and utilised corresponding electrodes in frontal and motor cortex areas (FC3, FC1, FCZ, FC2, FC4, CZ, CP3, C4, C3).

In set 2 of the EEG power data analysis, more specific elements of the DMN were explored. This included examining separately a cluster of electrodes of the posterior DMN and electrodes corresponding to the posterior cingulate cortex cluster (PCC Cz, C4), the precuneus cluster (O1, Pz, O2), and the temporal lobe cluster (P3, P4). The anterior DMN was explored through investigation of the ventromedial prefrontal cortex (vmPFC; Fp1, Fp2, Fz). These electrode selections were based upon recently verified topographical map and cluster suggestions from Giacometti et al. (2014) and in recent work in FND from Kozlowska et al., (2018).

7.3.4 Statistical analyses

Analysis of variance (ANOVA) was used to investigate differences in clinical measures between those with FND and healthy controls. An ANOVA was applied to explore differences in inflammatory markers (IL-6 and CRP) between the two groups (FND and Controls). A further ANOVA was run to consider covariates of Mood (Depression, Anxiety, Stress) and BMI. Pearson's correlations were then used to explore the relationship between IL-6 and CRP and Dissociation. With regard to EEG, MANOVA was performed to compare the cortical network characteristics at the global level and in each frequency band across the scalp. Bonferroni corrections and adjusted p-values were applied to control for multiple comparisons. Forms of cluster analysis were then run to explore frequency bands within clusters of electrodes at specific sites of interest using MANOVA. Again, upon completion, covariates of IL-6, CRP and Mood were added to the model. Correlations between inflammation data and EEG were applied using Pearson's correlations in each group and any significant comparisons made between these applied Fisher's Z to assess the magnitude of difference between the groups. All statistical analyses were performed in SPSS v28.

7.4 Results

7.4.1 Inflammation and psychological constructs: between-group comparisons

Table 8 shows the descriptive statistics, f-values and significance for the groups for Dissociation, Stress, Anxiety, Depression, BMI, IL-6 and CRP.

Table 8: Means, standard deviations and significance values for each of the tested variables for FND and Control Groups in Study 3, Chapter 7

	FND		Controls		*f statistic*	*95% CI*	*p*
Variables	$\bar{x}$	*SD*	$\bar{x}$	*SD*			
Anxiety	31.26	9.34	19.92	7.75	23.788	[23.436, 27.955]	**<.001**
Depression	32.39	12.07	19.56	5.81	23.149	[23.318, 28.639]	**<.001**
Stress	32.91	10.60	22.58	8.58	15.466	[25.343, 30.440]	**<.001**
BMI	30.19	6.34	26.78	4.98	5.067	[26.975, 29.996]	**.028**
Dissociation	68.29	17.92	43.48	8.93	36.870	[51.728, 59.424]	**<.001**
IL-6	.1675	.1126	.0786	.0341	17.051	[.190, .233]	**<.001**
CRP	.2404	.0885	.1822	.0947	7.478	[.102, .144]	**.008**

ANOVA was used to explore psychometric data obtained prior to physiological testing. The FND group scored significantly higher than healthy controls for Anxiety (p <.001), Dissociation (p <.001), Depression (p <.001) and Stress (p <.001). BMI was also significantly higher for the FND group than for the control group (p = .028) and thus was considered as a covariate in the analysis which follows.

7.4.2 Inflammation Findings

Multivariate analyses using ANOVA were used to explore the relationship between groups for inflammatory markers IL-6 and CRP to protect against Type II errors, which can occur from multiple t-test comparisons. The mean CRP index of the FND group (M = .2404, SD = .0884) was significantly higher than that of the Healthy Control group (M = .1822, SD = .0947; F (1, 76) = 7.478, p = .008). ANOVA was also used to explore the relationship between IL-6 and Group. The mean IL-6 index of the FND Group (M =.1675, SD = .1126) was significantly higher than that of the Healthy Control Group (M = .0786, SD = .0341; F (1, 76)

= 17.051, p <.001). These differences are displayed in Table 8 along with psychometric data and are displayed in Figure 3.

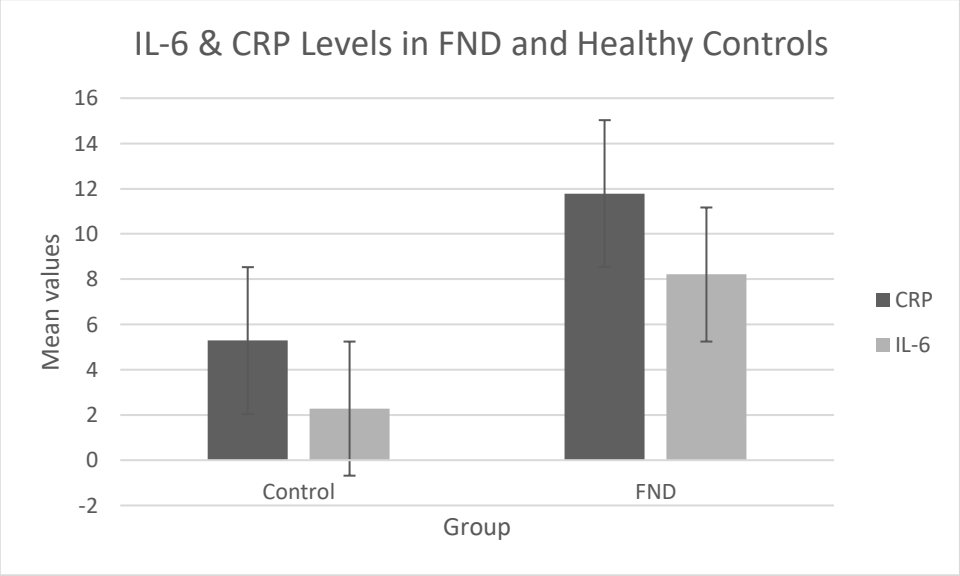

Figure 3: Levels of IL-6 and CRP in FND and Healthy Controls, Chapter 7, Study 3

A multivariate analysis of variance (MANOVA) with covarying factors was used to examine the independent effects of other variables in this relationship. This included examining the independent effects of BMI, Depression, Stress, and Anxiety as covariates in the relationship between group membership and IL-6 and CRP levels. MANOVA revealed significant differences in IL-6 levels between the FND and Control Groups (F (5, 64) = 5.195, p <.001), as indicated by a Type III sum of squares value of .212. However, no significant differences were found in CRP levels between the two groups (F (5, 64) = 1.395, p = .238), with a Type III sum of squares of .055.

Further examination of individual predictors revealed significant effects of Depression on IL-6 levels (F (1, 64) = 4.453, p = .039), but not on CRP levels (F (1, 64) =, p = .606). Additionally, BMI showed a marginal effect on CRP levels (F (1, 64) = 3.431, p = .060) but not on IL-6 levels (F (1, 64) = 1.877, p = .175). Group membership showed a significant influence on IL-6 levels ((F (1, 64) = 4.744, p = .033), but not on CRP levels (F (1, 64) = .926, p = .340). Stress and anxiety did not significantly influence IL-6 or CRP levels. Overall, the model accounts for a significant proportion of the variance in IL-6 levels (R^2 = .289, Adjusted

R^2 = .233) but only a small proportion of the variance in CRP levels (R^2 = .098, Adjusted R^2 = .028).

7.4.3 Dissociation and inflammation

Pearson's Correlation Coefficients were used to assess the relationship between Dissociation, IL-6 and CRP. In the total sample, significant positive correlations were found between CRP and IL6 levels (r = .387, p < .001), indicating a moderate positive relationship between these inflammatory markers. Additionally, there was a moderate, positive correlation between Dissociation and IL-6 levels (*r* = .285, *p* =.016) and Dissociation and CRP levels (*r* = .242, *p* =.042). Findings indicate that higher levels of inflammatory markers IL-6 and CRP are associated with greater levels of dissociation within the overall sample. Notably, when correlations were run for the FND group alone, similar patterns of associations were observed. Within the FND group, there were significant positive correlations between CRP and IL6 levels (*r* = .379, *p* = .007) and between CRP levels and dissociation (*r* = .149, *p* = .036), albeit the latter was weaker. Conversely, in the healthy control group, no significant correlations were found between CRP and IL6 levels (*r* = .105, *p* = .589) or between IL6 levels and dissociation (*r* = -.281, *p* = .206), and a negligible correlation was observed between CRP levels and dissociation (*r* = -.005, *p* = .983).

7.4.4 EEG Investigations at Midline Sites

These were investigated across the scalp at the frontal, frontocentral, centroparietal, temporal, and occipital regions. At lower frequency bands (Delta and Theta), there are no significant differences between FND and Healthy controls to report. The statistics associated with these tests can be seen in Table 9.

Table 9: Delta and Theta Frequency analysis in EEG at midline cites across the scalp, Chapter 7, Study 3

Site	Mean Value FND μV^2	Mean Value Control μV^2	F	p-value	Partial Eta Squared Effect Size
Delta					
Frontal	19.84	18.57	.802	.374	.012
Frontocentral	11.26	10.57	.619	.424	.009
Centroparietal	13.40	13.29	.029	.865	.000
Temporal	25.16	23.35	.821	.368	.012
Occipital	11.98	11.62	.115	.735	.002
Theta					
Frontal	9.25	8.64	.586	.447	.009
Frontocentral	5.93	5.54	.494	.484	.007
Centroparietal	6.75	6.58	.061	.806	.001
Temporal	11.33	10.47	.647	.424	.010
Occipital	6.01	5.79	.150	.700	.002

ANOVA also explored sites across higher frequency bands (Alpha, Beta and Gamma) and again across the scalp. Of note, those with FND had statistically lower alpha at frontocentral (p <.001), centroparietal (p <.001) and temporal (p =.46) sites in comparison to healthy controls. Mean scores for the FND group were also significantly reduced in the Beta frequency band at the centroparietal cluster (p = .035) and in the Gamma frequency band at the temporal cluster (p =.023). These results are displayed in Table 10.

Table 10: Alpha, Beta and Delta Frequency analysis in EEG at midline sites across the scalp, Chapter 7, Study 3

Site	Mean Value FND μV^2	Mean Value Control μV^2	F	p-value	Partial Eta Squared Effect Size
Alpha					
Frontal	7.36	8.06	.754	.388	.011
Frontocentral	4.98	7.09	19.041	**<.001**	**.224**
Centroparietal	6.09	8.98	16.711	**<.001**	**.202**
Temporal	10.05	12.33	4.155	**.046**	**.059**
Occipital	6.12	6.85	.745	.391	.011
Beta					
Frontal	5.11	4.87	.337	.564	.005
Frontocentral	3.20	2.96	.772	.383	.012
Centroparietal	3.50	4.18	4.631	**.035**	**.066**
Temporal	6.98	7.76	1.868	.176	.028
Occipital	3.22	3.05	.415	.522	.006
Gamma					
Frontal	1.75	1.635	.295	.589	.004
Frontocentral	.859	.738	1.814	.183	.027
Centroparietal	.759	.835	.735	.394	.011
Temporal	2.36	3.03	5.409	**.023**	**.076**
Occipital	.926	.877	.184	.670	.003

Note: Tests denoting significant differences have been bolded.

Activity across electrode sites and across frequency maps can be seen in Figure 4. The collection of 5-line graphs depicts activity across the scalp in relation to each frequency band. Whilst differences between those with FND and Healthy controls are often too small to be deemed of statistical significance, there is a general pattern of altered activity which requires further exploration.

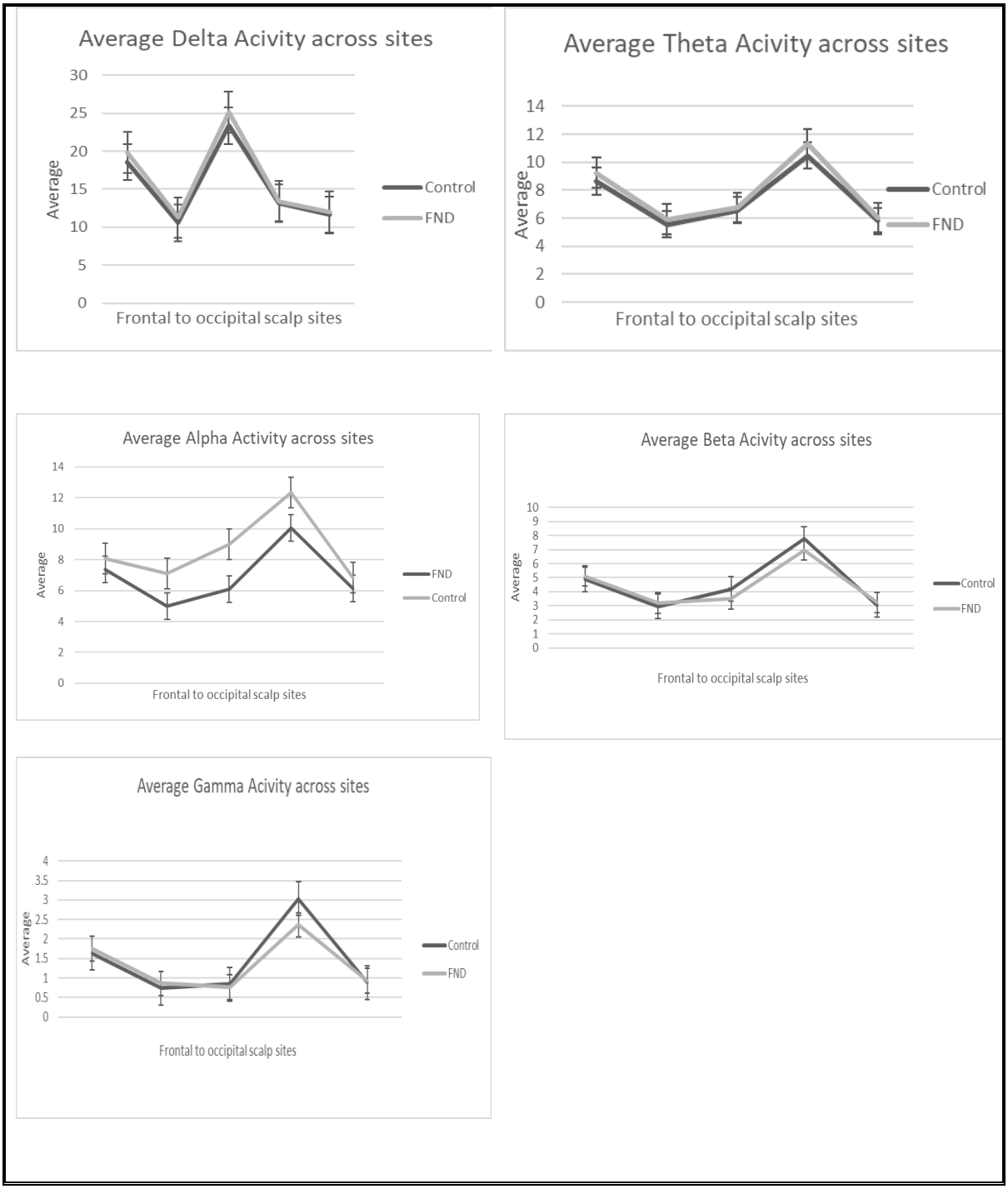

Figure 4: Denoting Average frequency bands across Frontal, Frontal central, Central Parietal, Temporal and Occipital regions across the scalp in FND and Control Groups

A repeated measures ANOVA was conducted to examine the effects of electrode clusters on EEG power across different frequency bands. The model included five within-subject factors representing electrode clusters (Frontal, Frontocentral, Centroparietal, Temporal, Occipital), and dependent variables representing EEG power in different frequency bands (Delta, Theta, Alpha, Beta, Gamma). Tests of between-subjects effects revealed a significant main effect of electrode clusters on EEG power across all frequency bands (Wilks'

= .199, f (68, 296) = 10.553, p <.001, ηP^2 = .728). Group was included as a between-subjects factor and revealed a significant main effect of group on EEG power across all frequency bands, Wilks' Λ = 0.399, F (1, 68) = 52.618, p < .001, partial ηP^2 = .437.

Analysis indicated that there was no significant effect of electrode clusters in delta (F (4, 296) = .029, p =.865). There was also no effect of Group found for delta (F (1, 68) = .802, p = .374, ηP^2 = .012). Similarly, there was no significant main effect of electrode clusters in Theta band power (F (4, 296) = .647, p =.424) and no effect of Group (p = .249).

MANOVA analyses here showed a significant main effect of electrode clusters on Alpha band power, (F (4, 269) = 19.041, p < .001, ηP^2 = .224). There was also a significant main effect of group on Alpha band power (F (1, 68) = 23.688, p = <.001, ηP^2 = .258 Post hoc analyses using univariate ANOVA showed significant variations in Alpha band power across different electrode clusters, particularly between frontal and frontocentral clusters (F (1, 269) = 68.989, p < .001, η^2 = .224). Analysis revealed a significant main effect of electrode clusters on Beta band power (F (4, 269) = 4.631, p = .035, ηP^2 = .066) and of Group (F (1, 68) = 7.131, p = .009, ηP^2 = .095). Contrasts between Frontocentral and Centroparietal electrode clusters showed significant differences in Beta band power (F (1, 269) = 7.223, p = .035, ηP^2 = .066). Analysis revealed a significant main effect of electrode clusters on Gamma band power (F (4, 269) = 5.409, p = .023, ηP^2 = .076). There was also a significant main effect of group on Gamma (F (1, 68) = 10.192, p = .002, ηP^2 = .130). Post hoc tests indicated specific differences among electrode clusters for Gamma band power, and there was a significant difference in Gamma between Temporal and Occipital electrode clusters (F (1, 269) = 7.098, p = .023, ηP^2 = .076).

7.4.5 Group differences in EEG spectral power in the DMN, Salience, SMA and Temporal and Parietal Clusters

Spectral power was examined in areas of interest outlined in the methods. Patients with FND showed increased Delta activity in the DMN, SMA and Temporal regions. No significant differences were noted in the Theta frequency band. These differences are noted in Table 11.

Table 11: Delta and Theta Frequency analysis in DMN, Salience, SMA and Lateral Parietal and Temporal Clusters, Chapter 7, Study 3

Site	Mean Value FND μV^2	Mean Value Control μV^2	F	p-value	Partial Eta Squared Effect Size
Delta					
DMN	2.81	2.13	16.646	**<.001**	**.201**
Salience	2.77	2.68	.260	.612	.004
SMA	2.27	1.63	21.793	**<.001**	**.248**
Temporal	2.67	2.25	10.296	**.002**	**.135**
Theta					
DMN	1.17	1.14	.135	.715	.002
Salience	1.28	1.22	.410	.524	.006
SMA	.973	.951	.089	.766	.001
Temporal	1.13	1.11	.058	.810	.001

Note: Tests denoting significant differences have been highlighted in bold.

Those with FND also showed reduced activity in Salience and SMA networks in Alpha frequency and reduced Beta activity in the SMA and Temporal regions. Further analysis also revealed differences in Gamma activity particularly in the DMN, SMA and Temporal clusters. These findings are noted in Table 12.

Table 12: Alpha, Beta and Delta Frequency Analysis in DMN, Salience, SMA and Lateral Parietal and Temporal Clusters, Chapter 7, Study 3

Site	Mean Value FND μV^2	Mean Value Control μV^2	F	p-value	Partial Eta Squared Effect Size
Alpha					
DMN	1.16	1.12	.137	.713	.002
Salience	.945	1.38	21.958	**<.001**	**.250**
SMA	.795	1.25	29.297	**<.001**	**.307**
Temporal	1.12	1.31	2.441	.123	.036
Beta					
DMN	.688	.649	.156	.694	.002
Salience	.755	.724	.234	.630	.004
SMA	.515	.704	7.999	**.006**	**.108**
Temporal	.663	.848	8.384	**.005**	**.113**
Gamma					
DMN	.182	.442	33.384	**<.001**	**.336**
Salience	.271	.256	.197	.659	.003
SMA	.136	.186	7.089	**.010**	**.097**
Temporal	.212	.304	10.491	**.002**	**.137**

Note: Tests denoting significant differences have been bolded.

7.4.6 Relationships between DMN, Salience, SMA and Temporal Networks in Relation to Groups, Inflammation and Dissociation

A MANOVA was conducted to investigate the impact of DMN, Salience, SMA, and Temporal clusters of EEG activity on various frequency bands (Delta, Theta, Alpha, Beta, and Gamma) in relation to groups with CRP, IL6, and Dissociation serving as covariates. The analysis revealed a significant multivariate effect of network clusters on frequency power, indicating that the combined clusters significantly predicted variations across the different frequency bands (Wilks' Lambda = .647, F (16, 240) = 3.268, p <.001, ηP^2 = .179). Specifically, within the Delta frequency band, the DMN cluster showed significantly higher EEG power compared to other clusters (F (4, 240) = 7.548, p < .001, ηP^2 = .346), indicating increased activity in regions associated with the DMN during restful states. In the Alpha

frequency band, both the Salience and SMA clusters exhibited significantly higher EEG power compared to other clusters (Salience: F (4, 240) = 4.858, p = .002, ηP^2 = .254; SMA: F (4, 240) = 5.819, p < .001, ηP^2 = .290), suggesting enhanced attentional and motor processing, respectively, in these regions. Furthermore, in the Gamma frequency band, the DMN cluster demonstrated significantly higher EEG power compared to other clusters (F (4, 240) = 12.061, p < .001, ηP^2 = .458), indicative of increased neural synchronisation associated with cognitive processing.

Univariate ANOVAs for each band demonstrated significant main effects for these clusters in all frequency bands, and Tables 11 and 12 note where these were significantly different between groups. When mediated by covariates, within the Delta frequency band, the group differences were particularly pronounced, with significant effects observed for all clusters (DMN: F (1, 240) = 27.125, p < .001, ηP^2 = .322; Salience: F (1, 240) = .992, p = .323, ηP^2 = .017; SMA: F (1, 240) = 18.986, p < .001, ηP^2 = .250; TNP: F (1, 240) = 3.492, p = .067, ηP^2 = .058), suggesting distinct neural processing patterns between groups, possibly related to cognitive or affective states. Notably, in the Alpha frequency band, significant group differences were observed in the Salience and SMA clusters (Salience: F (1, 240) = 11.407, p = .001, ηP^2 = .167; SMA: F (1, 240) = 11.326, p = .001, ηP^2 = .166), indicating differential attentional and motor processing across groups. Similarly, in the Gamma frequency band, significant group differences were found in the DMN and TNP clusters (DMN: F (1, 240) = 23.651, p < .001, ηP^2 = .293; TNP: F (1, 240) = 5.618, p = .021, ηP^2 = .090), suggesting distinct patterns of neural activity.

The results revealed significant main effects for IL-6, CRP, and dissociation, as well as significant interactions between these factors and electrode clusters within specific frequency bands. Specifically, or delta, significant main effects were observed for IL-6 (p <.001, ηP^2 = .336), CRP (p =.40, ηP^2 = .159), and dissociation (p =.007, ηP^2 = .112). These effects varied across different electrode clusters, indicating differential modulation of EEG power as influenced by inflammatory markers and dissociative symptoms. Specifically, TNP cluster differences in the Delta frequency band were moderated by CRP levels (F (4, 240) = 2.692, p = .040, ηP^2= .159).

Additionally, in the alpha frequency band, significant main effects were found for IL-6 (p = .002, ηP^2 = 2.54) and CRP (p <.001, ηP^2 = .290), suggesting their influence on neural oscillations within specific brain regions. Analysis revealed a significant main effect of group

on Beta band power (F (1, 68) = 7.131, p = .009, ηP^2 = .095). Differences in Alpha band within the salience cluster were influenced by IL6 levels (F (4, 240) = 4.858, p = .002, ηP^2 = .254). Additionally, dissociation showed a significant main effect (p = .037, ηP^2 = .166), indicating an association with alterations in alpha band activity. This specifically moderated differences in Beta within the DMN cluster (F (4, 240) = 7.939, p = .007, ηP^2 = .122). Finally, CRP levels were found to have moderate differences in the Gamma frequency band; this was particularly noted within the SMA cluster (F (4, 240) = 2.567, p = .048, ηP^2 = .153).

7.4.7 Exploration of areas within the DMN in relation to frequency bands

Final multivariate analyses explored specific facets of the DMN; notably, these were explored by clusters of electrodes to denote the Posterior Cingulate Cortex (PCC), Precuneus, ventromedial Prefrontal Cortex (vmPFC) and Temporal Lobe cortex (TLC). Group differences are explored in relation to frequency bands (Delta, Theta, Alpha, Beta and Gamma) and in relation to the group. In relation to Delta and Theta activity, the FND group showed higher activity in the PCC Precuneus and vmPFC. No differences were noted in Theta. Results are displayed in Table 13.

Table 13: Delta and Theta Frequency analysis in DMN components (PCC, Precuneus, vmPFC and Temporal Lobe), Chapter 7, Study 3

Site	Mean Value FND μV^2	Mean Value Control μV^2	F	*p-value*	R^2
Delta					
PCC	3.77	3.01	8.761	**.004**	**.117**
Precuneus	6.92	5.38	7.490	**.008**	**.102**
TLC	3.76	3.75	.002	.963	.000
vmPFC	9.10	7.06	9.807	**.003**	**.129**
Theta					
PCC	1.93	1.80	.484	.489	.007
Precuneus	3.45	3.42	.020	.889	.000
TLC	1.89	1.83	.080	.778	.001
vmPFC	4.32	3.95	.595	.443	.009

Note: Tests denoting significant differences have been highlighted in bold.

In relation to Alpha activity, the FND group showed lower activity in the PCC, Precuneus and vmPFC. The FND group also showed lower activity in the vmPFC in the Gamma Frequency band and a trend toward significance in TLC. No significant differences were noted in Beta. These statistical analyses are outlined in Table 14.

Table 14: Alpha, Beta and Delta Frequency Analysis in DMN components (PCC, Precuneus, vmPFC and Temporal Lobe), Chapter 7, Study 3

Site	Mean Value FND μV^2	Mean Value Control μV^2	F	*p*-value	R^2
Alpha					
PCC	1.59	3.64	51.913	**<.001**	**.440**
Precuneus	2.46	5.22	61.616	**<.001**	**.483**
TLC	1.93	2.38	2.614	.111	.038
vmPFC	2.89	3.93	12.793	**<.001**	**.162**
Beta					
PCC	1.01	.942	.513	.476	.008
Precuneus	1.88	1.80	.279	.599	.004
TLC	1.039	.956	.825	.367	.012
vmPFC	2.09	2.03	.125	.725	.002
Gamma					
PCC	.25	.21	2.287	.135	.033
Precuneus	.54	.51	.177	.675	.003
TLC	.25	.21	3.891	.053	.056
vmPFC	.49	.91	25.408	**<.001**	**.278**

Note: Tests denoting significant differences have been highlighted in bold.

The MANOVA reveals significant between-subject effects, as evidenced by the corrected model's statistical significance (F (1, 67) = 8.761, p = .004, R^2 = .117), indicating overall predictive power. Subsequent examination of group differences elucidates noteworthy variations in neural activity in different brain network regions and frequency bands, noted in Tables 13 and 14. These are particularly evident in the Delta, Alpha, and Gamma frequency bands.

7.4.8 Interactions between *PCC, Precuneus, vmPFC and Temporal Lobe* in Relation to Groups, Inflammation and Dissociation

An additional MANOVA was run for these clusters to include IL-6, CRP and Dissociation as well as a group, and this was statistically significant (Wilks' Lambda = .596, F (20, 206) = 2.135, p = .006). This indicates that the combined set of covariates significantly predicted the cluster variables. For the delta frequency band, significant corrected models based on these covariates were found for PCC (F (4, 57) = 3.582, p = .011, R^2 = .201), and Precuneus showed a trend toward significance (F (4, 57) = 2.518, p = .051, R^2 = .150). In delta, there was also a significant effect observed for the corrected model in the vmPFC cluster (F (4, 57) = 4.545, p = .003, R^2 = .201). Group had a significant effect in this corrected model for PCC (F (1, 57) = 6.694, p = .012, R^2 = .285), Precuneus cluster (F (1, 57) = 8.027, p = .006, R^2 = .285) and vmPFC (F (1, 57) = 16.824, p <.001, R^2 = .150), suggesting its influence on these clusters in the Delta band.

Similarly, in the Alpha frequency band, significant corrected models were observed in the PCC (F (4, 57) = 11.631, p <.001, R^2 = .449), the Precuneus cluster (F (4, 57) = 14.233, p <.001, R^2 = .500) and the vmPFC (F (4, 57) = 2.897, p =.030, R^2 = .169). Group significantly influenced PCC (F (1, 57) = 27.364, p <.001, R^2 = .411), Precuneus (F (1, 57) = 8.761, p = .004, R^2 = .117) and vmPFC (F (1, 57) = 5.281, p =.025) clusters in the Alpha band. The Gamma frequency band showed significant corrected models in the vmPFC region (F (4, 57) = 7.705, p <.001, R^2 = .281). This was also observed as a significant effect in the exploration of the influence of Group (F (1, 57) = 12.242, p <.001). In the theta and Beta frequency bands, none of there were no significant observed effects for models or Groups, indicating a lack of relationship between covariates and clusters in these bands.

In exploring the influence of covariates, CRP levels exhibited significant effects on neural oscillations in the PCC region in both the Delta (F (1, 57) = 4.662, p =.035) and Gamma (F (1, 57) = 4.032, p =.049) frequency bands. IL6 showed no significant associations with these network clusters but showed a trend toward significance in PCC in both Delta (F (1, 57) = 3.298, p =.075) and Gamma (F (1, 57) = 3.385, p =.071). Dissociation as a covariate showed a significant relationship with vmPFC in Delta (F (1, 57) = 5.844, p =.019) and a trend toward significance for vmPFC in Theta (F (1, 57) = 3.326, p =.073).

7.4.9 Correlations between EEG, Dissociation and Inflammation

Whilst Dissociation and inflammation have been used as covariates throughout these electrophysiological analyses, Pearson's correlations were run to assess a more direct relationship with these measures and to ascertain the strength and direction of their influence. Whilst CRP did not correlate with any of the neural network clusters, there was a trend toward significance between CRP and the temporal and parietal region in Beta (r =.295, p = .052) and between CRP and the PCC in delta activity (r = .293, p = .054). IL-6 did not show any significant associations with any of the electrode clusters at any frequency sites. This indicates that a complex interplay and relationship may be present in the relationship between inflammation and neural activity in FND. Dissociation showed a strong negative correlation with DMN in Delta (r = -.418, p = .005) and DMN in alpha (r = -.319, p = .035). When exploring components of the DMN, Dissociation showed negative, significant correlations with vmPFC region in both Delta (r = -.359, p =.017) and Theta (r = -3.06, p = .043) frequency oscillations.

7.5 Discussion

This study aimed to explore inflammation, dissociation and brain function within FND. The study aimed to overcome the limitations of previous research by exploring more stable biomarkers indicative of inflammation and by including a multimodal research design which included psychological, physiological, neurochemical and electrophysiological data. It was hoped that integrating these findings would enable the consideration of more holistic findings in FND. Specifically, this study aimed to; 1) Explore differences in inflammatory markers (IL-6 and CRP) in FND compared to healthy, matched controls, 2) Consider the role of psychological and physiological data and their influence in inflammation, including if inflammatory levels are maintained when mediations for anxiety, depression, stress, BMI and dietary inflammation are considered, 3) explore inflammatory markers as correlates with dissociation 4) explore baseline EEG measures and their association with dissociation and inflammation in FND.

Inflammation, as measured by IL-6 and CRP, was found to be higher in those with FND than in healthy-matched controls. The findings presented within this study highlight that FND

goes beyond neural networks and that there are likely key inflammatory markers involved in this relationship. Much of the previous research in this field has focused on cortisol, but these have shown mixed results and variable methods (Apazoglou et al., 2017; Bakvis et al., 2009; Chung et al., 2023; Weber et al., 2024). Further, whilst this research is important, cortisol as a cytokine lacks specificity, and thus, the addition of findings presented here from more widely recognised and stable trait markers of inflammation (IL-6 and CRP) add to this body of literature and support the establishment of consideration of these markers and the role of neuroinflammation in FND.

Higher inflammatory levels remained even when covariates (depression, anxiety, stress, BMI) were considered in the model for IL-6 but not for CRP. CRP was particularly influenced by physiological measures (such as BMI) and psychological measures, particularly Depression. It is widely recognised that inflammation and concertation of cytokines can affect many physiological and psychological processes (Becher et al., 2017; Levin & Godukhin, 2017; McAfoose & Baune, 2009; McKim et al., 2016; Osipova et al., 2018). In addition to their role in the immune system, IL-6 and CRP are influenced by a wide range of factors, including psychological stress and physical activity (Petersen & Pedersen, 2005). Whilst IL-6 is involved in the initiation of the inflammatory cascade, CRP is a downstream marker of inflammation and is often considered a marker of systemic inflammation (Pepys & Hirschfield, 2003). Depression has been consistently associated with alterations in immune system function and increased inflammation (e.g., Miller et al., 2009). Chronic stress and depressive symptoms can dysregulate the HPA axis and nervous system, then leading to increased production of pro-inflammatory cytokines like IL-6. Moreover, depression is associated with changes in health behaviours (poor diet, physical inactivity) and physiological factors (dysregulated cortisol) that can further exacerbate inflammation (Miller, 2009). CRP, as a downstream marker of inflammation, may be particularly sensitive to these effects of depression due to its direct association with IL-6 production. Unlike IL-6, which is primarily regulated at the transcriptional level in response to various stimuli, CRP production is influenced by multiple factors, including genetic predisposition, environmental factors, and chronic diseases (Khera et al., 2005). Studies have shown that depression can directly influence CRP levels through its effects on hepatic function, insulin resistance, and adiposity (Howren et al., 2009). Additionally, depression-related behaviours such as poor sleep quality and substance abuse may contribute to increased CRP production independently of IL-6 levels (Howren et al., 2009). It is important to note, therefore, that the findings do not discredit the role of

inflammation in FND, but that reduced activity caused by mobility impairments or fatigue or overlap of symptoms, which lends to reduced quality of life and depression, could explain increases in CRP and the mediation between CRP and depression in FND. The persistence of elevated IL-6 levels, even when accounting for covariates, underscores its robustness as a biomarker and suggests a pivotal role of chronic inflammation in the pathogenesis of FND.

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Dissociation was found to correlate with both IL-6 and CRP in FND but not in healthy controls. This likely is because there were extreme levels and variability of dissociation in the FND, compared to the baseline levels reported by healthy controls. This finding aligns with previous studies, reinforcing the consideration of dissociation as a core feature in FND symptomatology. The relationship between dissociation and inflammation in FND could be bidirectional. While dissociation can influence inflammatory levels, inflammation itself can also induce dissociative experiences. Pro-inflammatory cytokines, such as IL-6, can cross the blood-brain barrier and affect neurotransmitter metabolism, potentially leading to behavioural

changes, including dissociation (Kronfol & Remick, 2000; Van Dyken & Lacoste, 2018). Psychological processes and the nervous system and immune responses are deeply interconnected. So, whilst dissociation can influence levels of inflammation in FND, heightened inflammation can likewise induce dissociative experiences.

In the context of FND, the principles of allostasis (Sterling, 1988) suggest that chronic stress and the resultant allostatic load can lead to dysregulation across multiple physiological systems, contributing to both heightened dissociation and inflammatory responses. These dysfunctions result in detrimental effects of allostatic load (McEwen, 2003), subsequently impacting other physiological and neural systems, which may play a role in the dysfunctions observed in FND. Dissociation has been implicated in this process and is increasingly considered to be a psychobiological reaction to allostatic overload (Grassi-Oliveira et al., 2008; Lamb et al., 2021; Staniloiu et al., 2010). However, while I do not ordinarily engage in quite so much intellectual fencing with myself, the complexity of this discussion (and the inherent limitations of inferring causality) demands a certain degree of counterbalancing contradiction. Indeed, the relationship between dissociation and inflammation is likely bidirectional, as inflammation itself may contribute to neurobiological changes that facilitate dissociative experiences. Pro-inflammatory cytokines, such as IL-6, have been shown to influence neurotransmitter metabolism and neural connectivity, potentially inducing alterations in consciousness and self-perception, which are core aspects of dissociation.

Further supporting the complexity of this model, Keynejad et al. (2019) explored allostatic load in FND using an index of 11 biomarkers, including metabolic, cardiovascular, inflammatory, HPA, and autonomic nervous system activity. Their findings particularly implicated elevated IL-6 and CRP alongside lower cortisol, reinforcing the role of systemic inflammation and dysregulated stress responses in FND. The present study's findings add to this body of research by demonstrating significant associations between dissociation and inflammatory markers, suggesting systemic and chronic inflammation should be integrated into theoretical models of FND. Given the complex interplay between immune and neurocognitive processes, further research is needed to clarify the directionality of these relationships and determine whether inflammation acts as a trigger, consequence, or reciprocal mechanism in dissociation and FND pathology.

In explorations of electrophysiological data in this study, there were notable areas of difference in FND in higher frequency bands (Beta, Alpha, Gamma) but nothing of note at

lower frequency bands (Delta and Theta). At higher frequency bands, patients with FND showed a lower frequency at the frontocentral, central and parietal regions. Previous research into children with FND found that there was excessive theta and delta power in electrode clusters, which corresponded to posterior rather than frontal regions (Kozlowska et al., 2018). Differences between the current findings and previous research could indicate differences in the neurobiology of FND between children and adult samples and previous research does note that symptoms display differently between these two populations (Vassiopoulos et al., 2022; Yong et al., 2023). Other research has noted that there are also alterations in frontal and central regions in children with FND using ICA data-driven approaches (Rai et al., 2022) which supports the findings of the current study.

Further exploration of EEG data in this study revealed that whilst Delta was not significantly different in overall scalp sites, there were differences in specific cluster areas. Specifically, the supplementary motor area and temporal areas showed alterations in different frequency bands. Beta frequency was increased in these areas, and gamma was decreased, indicating increased neural synchronisation in motor cognition and processing. This was supported by findings of reduced alpha in the salience area and SMA, which would indicate enhanced attentional and motor processing in FND. The differences between groups noted here indicate differences in attention and motor cognition in FND and distinct patterns of neural activity in FND. Support for these findings can be drawn from a range of neuroimaging studies in the past decade, which has highlighted that arousal, emotion processing and self-referential functions and attention are altered in FND (e.g., Voon, 2014; Vuilleumier, 2014; van der Kruijs et al., 2014). Studies of resting-state data in FND have also noted changes in functional network organisation in regions of the DMN, salience network and SMA which suggest activation of allostatic brain systems which shift to a more defensive brain organisation. This organisation is associated with increased arousal and attention in a system which prioritises reflective and defensive patterns over voluntary and motor control, which enables responses to threats to occur more rapidly (Arnsten, 2009; Kynazev et al., 2007). Additionally, CRP moderated delta in the temporal and parietal region and in the gamma region of the SMA. Il-6 showed wider effects, particularly in the alpha and beta salience clusters. Dissociation was seen to mediate this relationship too, particularly in the SMA. Combined, these findings suggest that inflammation mediates these networks and is further reflective of a system in which allostatic load has been increased, affecting emotional arousal and leading to reduced neural activity, which reflects a neural system in a defensive state.

Given findings attributed to the DMN, a further cluster was explored, which specifically focused on component parts of the DMN, including the PCC, Precuneus and vmPFC. Findings suggested that alpha frequency was reduced in some clusters and gamma was particularly reduced in the vmPFC for those with FND. There was a particular role of CRP in these neural oscillations particularly in the PCC in Delta and Gamma frequencies. A trend was noted for IL-6 in the same areas. Whilst correlations were noted for CRP and IL6 by themselves they were not significant. Taken together, findings here further emphasise that CRP levels in FND may be influenced by psychological measures such as depression and dissociation and, importantly, that inflammation levels influence neural activity in FND. They also demonstrate the complex interplay between these specific mechanisms and the activation of immune and inflammatory cells in changes to neuroplasticity and brain networks (Milligan & Watkins, 2009). Similarly, the brain's immune effector cells (glial cells) may be particularly influenced by inflammation and psychological measures of distress and dissociation, which may contribute toward increased and decreased neural activity in the brain at rest in specific sites (Fields, 2009; Frank et al., 2016; von Bernhardi et al., 2016).

Dissociation was found to have particular influences on the vmPFC in the delta and theta and in DMN activity in the delta and alpha band. This aligns with existing literature on the neurobiological underpinnings of FND. Studies have consistently implicated alterations in the function and connectivity of the vmPFC and DMN in the pathophysiology of FND (Hassa et al., 2021; Voon et al., 2016). The vmPFC is involved in emotion regulation and self-referential processing, whist the DMN is associated with introspection and self-awareness. Dysfunctions in these regions have been proposed to contribute to the cognitive and affective symptoms characteristic of FND, including dissociation (Hassa et al., 2021; Voon et al., 2016). The specific effects of dissociation on delta and theta oscillations in the vmPFC and delta and alpha oscillations in the DMN provide further insights into the neurophysiological mechanisms underlying dissociative experiences in FND. Delta and theta oscillations are associated with deep states of relaxation, introspection, and altered states of consciousness, while alpha oscillations are related to attentional processes and cognitive control (Kleckner et al., 2017; Knyazev, 2012). Dysregulated oscillatory activity in these frequency bands may reflect disruptions in neural communication and synchronization within and between brain networks, contributing to the manifestation of dissociative symptoms in FND. These findings can be integrated into existing neurobiological models of FND that emphasise the role of dysfunctional self-awareness, emotion regulation, and cognitive control processes (Edwards et

al., 2008; Voon et al., 2016). Dissociation, characterised by disruptions in consciousness, identity, and memory, may arise from aberrant processing within the vmPFC and DMN, leading to a disconnection between self-referential processing and external reality. Importantly, these neural alterations may interact with psychological and environmental factors to perpetuate and exacerbate dissociative symptoms in FND (Hassa et al., 2020; Perez et al., 2018).

The findings demonstrate that the conceptualisation of FND should go beyond that of a neural network disorder and that FND should be considered as a "whole body" or embodied brain disorder. Previous research has highlighted how biological markers and bodily dysfunctions could underpin neural network dysfunctions (Asadi-Pooya, 2016; Milano et al., 2023; Villagrán et al., 2021). The current study adds to this argument further and considers that psychological states like dissociation and biological dysfunction, including inflammation, underpin neural network dysfunction in FND. Whilst, of course, the current study cannot determine cause and effect, it is essential to note the relationships between these markers. FND could be considered a product of dysfunction in neuroinflammation, wherein chronic inflammation has led to impaired neural networks. Further, the findings could explain crash slump reactions in FND. It may also lend toward exploration and consideration of treatment, which targets not only neural networks but also reduces dissociation and inflammation. Breaking the bidirectional cycle in which these constructs operate could lead to significant changes in quality of life, psychological distress and symptom reduction. Additionally, dissociation must be considered in overall functional outcomes in those with FND and identification of neural biomarkers associated with dissociation could aid the early detection and diagnosis of FND, facilitating timely intervention and personalised treatment planning to improve symptom outcomes.

This study is not without its limitations. Firstly, the distribution of those with FND and healthy controls is slightly skewed, and additional controls could have enabled a more robust design. In relation to inflammation, whilst ELISA assays are sensitive and widely used for quantifying protein concentrations, they may have limitations in specificity as cross-reactivity with other proteins or interference of biological samples could affect the accuracy of the measurements. Care was taken to ensure that factors such as batch-to-batch variability and sample handling procedures were rigorous and that standardised assay protocols were followed. However, future research could explore alternative assay techniques, including multiplex immunoassays or mass spectrometry-based approaches, to validate findings and

explore distributions between different markers. ELISA assays provide quantitative measurements of IL-6 and CRP levels but not of underlying biological mechanisms driving changes in inflammation. Future research could also incorporate complementary molecular and cellular techniques, including gene expression analysis or immunohistochemistry, to investigate the molecular pathways and cellular processes associated with alterations in inflammatory markers in FND.

In relation to EEG, whilst comprehensive, additional techniques could have been applied to the data to add several important dimensions to the findings and address some of the present limitations. ICA is a powerful technique for decomposing EEG data into spatially independent components and representing distinct brain networks or sources of neural activity (Makeig et al., 1997), and this was not applied here. This could support the investigation of brain networks associated with inflammation and dissociation and enable the examination of dynamics and interactions to provide a more comprehensive understanding of neural correlates and neurobiological mechanisms. Additionally, dipole modelling was not applied which could enable estimation of the location and orientation of electrical sources based on EEG scalp recordings. Findings, particularly of the vmPFC and DMN regions in his study, should, therefore, be interpreted with caution. Additionally, EEG does have a limited spatial resolution in comparison to over-neuroimaging techniques, and further investigations with fMRI could further support the findings and explore the spatial distribution of neural activity. Similarly, advanced EEG processing such as the application of Spiking Neural Networks (SNN) to explore differences in connectivity throughout brain data which should be considered in future research.

Finally, whilst this study identified associations between inflammation and FND and considered the role of neural networks and markers of psychological constructs like mood and dissociation, further research is needed to draw clear conclusions. The cross-sectional nature of the design limits the ability to draw causal inferences or assess temporal relationships. Future research could employ longitudinal study designs to investigate the interplay between these dynamics in FND over time. Additionally, an important future direction would be the inclusion of a long-term disorder (LTD) comparison group to determine whether the inflammatory, neural, and psychological profiles observed here are unique to FND or reflective of chronic illness more broadly. Given the exploratory and feasibility-driven nature of this study, the inclusion of an additional LTD group was beyond the scope of the available resources, time and funding, particularly given the complexity of EEG and phlebotomy-based data collection.

However, future studies should aim to systematically compare FND with other chronic conditions systematically, and this would enhance our ability to differentiate disorder-specific mechanisms from those arising from chronic health burden. Furthermore, an examination of the potential clinical correlates, including symptom clusters (as identified in Chapter 6), symptom severity, treatment response or functional outcomes, could provide valuable insights into the clinical relevance of inflammatory markers in FND. Finally, EEG analyses hold promise for further defining subtypes of FND, as they have been successfully employed in other conditions, such as ADHD (e.g. Clarke et al., 2001).

7.6 Chapter Summary

Chapter 7 has explored the role of inflammation and neural network dysfunction in FND. In particular, it highlights the complex interplay between inflammation, neural networks, baseline frequency data and dissociation in FND. Whilst this study is not without limitations, it provides key findings which enhance the understanding of FND as a condition of allostatic load and findings are related to conceptualisations of FND as an embodied brain disorder, one in which there are alterations to physiology, psychology and neural network activity. This is explored further in the final chapter, Chapter 8, which provides an overall discussion of all the findings of this thesis.

Chapter 8: General Discussion

8. 1 Thesis overview

The current thesis seeks to understand FND regarding the neurophysiological and neuropsychological mechanisms that may underpin the disorder. The first chapter explored definitions and the history of the development of the conceptualisation of FND. It challenged this with Chaos theory and slump crash reactions, often overlooked as part of FND. Chapter 2 explored the psychological correlates of FND and mainly focused on dissociation, which may warrant further investigation into FND and inclusion in theoretical models. This was followed by Chapter 3, which provides a detailed description of the neurophysiology and neurochemical correlates of FND. From these discussions, a series of questions were formulated and addressed throughout this thesis:

1. Is dissociation a core construct in FND, and how does this relate to other psychological correlates of chronic illness (stress, anxiety, depression, resilience, social isolation and social support) and outcomes (cognitive flexibility, hopefulness)?
2. Can the presence of potential subtypes of FND be statistically identified through LCA analysis, and what are their relationships to dissociation types and predisposing factors?
3. What is the role of inflammation in FND, and how does this relate to dissociation?
4. Is inflammation in FND mediated by other facets of chronic illness, including dietary inflammation, BMI and mood?
5. Do baseline EEG measures and Default Mode Network (DMN) differ in FND?
6. What is the relationship between neural activity at baseline, inflammation and dissociation in FND?

Chapter 5, the first empirical chapter, undertook primary investigations into the role of dissociation in FND. The aim was to establish its appropriateness as a measure and its relation to symptom outcomes and other measurable constructs in FND. The findings were significant, suggesting that multiscale FND constructs were suitable for investigating FND. Moreover, these constructs exhibited distinct differences between healthy controls and individuals with other long-term conditions. Elevated dissociation in FND was particularly relevant across five constructs (Derealisation, Memory, Emotional, Disengagement and Depersonalisation) but not for identity. Elevated dissociation in FND was not mediated by trauma, mood or social isolation, suggesting that this may be a particular area of dysfunction in FND that is distinct

from other long-term chronic illnesses and which warranted further investigation. Dissociation did, however, display a relationship with cognitive flexibility, suggesting that dissociation impairs this ability and should be explored with neurobiological measures to assess the role of dissociation on neural activity. This underscores the importance of considering dissociation in subsequent investigations, as hinted by the research findings.

Before such investigations, the question of whether there are discernible subtypes in FND was addressed in Chapter 6. As previous research has noted differences in psychological and neurobiological function for different subtypes, it was felt that it was essential to see if symptoms could be clustered into theoretically viable and statistically meaningful categories. Findings of between-group comparisons in LTD, FND and Healthy controls supported the findings from Chapter 5. They contributed new findings highlighting the role of cognitive flexibility and impairments in quality of life in FND. Without a scale of FND, literature was consulted to develop a list of commonly reported symptoms. Through latent class analysis (LCA), a 7-class model based upon these symptoms was identified. Clusters were named based on theoretical overviews of the prevailing symptoms; these were: Motor Dissociation States, Non-Responsive Tremor, Polysymptomatic Seizure, Occasional Neuropathic, Mixed Multisystem symptoms, Intermittent Seizure-Movement and Occasional Dystonic. These seven subtypes were further explored regarding additional (non-core) symptoms through LTA. Consideration was also given to relationships between the identified subtypes, predisposing or triggering events and dissociation. These additional considerations enabled further characterisation of the subtypes of FND, and the distinct profile of each was noted. This exploratory study required further validation, so it was not carried over to Chapter 7.

Chapter 7 presents a final empirical multimodal study to explore inflammation in FND and combined analysis of EEG resting state data and dissociation. Inflammatory markers (IL-6 and CRP) were higher in those with FND than in healthy controls. Whilst IL-6 levels remained even when covariates (Stress, Anxiety, Depression, Dissociation, BMI) were considered, CRP levels did not. This indicates the role of different inflammatory pathways in the pathogenesis of FND. CRP was mainly influenced by depression, highlighting that adverse effects of chronic illness could, in part, be associated with psychobiological constructs and perhaps as a consequence of previously noted reductions in quality of life. Additionally, EEG resting-state data revealed altered neural activity in FND, particularly at midline and Default Mode Network (DMN) sites, suggesting disruptions in intrinsic neural connectivity. The relationships between altered patterns of activity were extremely specific and dependent upon

the frequency oscillation being explored, with the greatest differences seen in higher frequency bands. Relationships between dissociation and EEG activity were also observed, with either higher dissociation scores associated with abnormal oscillatory activity in key cortical regions, reinforcing the role of dissociative processes in shaping functional neural alterations in FND. These findings are explored in greater depth in chapter 7 and later in this discussion.

The current chapter discusses these findings and how they contribute to furthering our understanding of FND. Additionally, the methods used are discussed in their relation to FND and the findings' contributions to theoretical models and treatment. Finally, the limitations are discussed alongside avenues for future research.

8.2 Dissociation

Dissociation, in its broadest sense, describes a loss of integration of typically integrated cognitive functions. Conceptualisations of dissociation usually consider a loss of awareness of cognitive or physical processes and represent a state of altered consciousness (Goldberg, 2020; Lanius, 2015). The conceptualisation of this construct has not been without controversy, and more recent conceptualisations of dissociation consider it is a multifactorial measurement (e.g., Briere et al., 2005; 2016; Holder, 2013) and to be more about the identification of types of dissociation rather than a sum of dissociative experiences. Throughout the thesis, dissociation is considered as both a multifactorial and a unitary model in places to enable a rich depth of exploration in FND. Dissociative pathology has been studied across a range of psychological and neurological disorders, including Schizophrenia, Epilepsy, multiple sclerosis and post-traumatic stress disorder (PTSD; Armour et al., 2014; Bob & Mashour, 2011; Medford, 2014; Scarrabelotti & Carroll, 1999). However, little attention has been given to its potential role in FND.

Despite the overlap of symptoms of dissociative experiences and their frequent reports in those with FND, little previous research has explored this. Furthermore, pathological dissociation should be considered across illnesses (Hunter et al., 2003; Medford et al., 2003), particularly as dissociation is an essential predictor across illnesses for poor treatment responses and high relapse rates and contributes toward the likelihood of development of severe mental ill-health, chronic symptoms or additional disabling symptoms as a byproduct of elevated levels of dissociation (Bailey & Brand, 2017; Cronin et al., 2014; Halvorsen er al.,

2014; Spitzer et al., 2007; Thompson-Hollands et al., 2017). Throughout this thesis, dissociation was considered as both a byproduct and a symptom of FND. Despite the mirroring of histories between dissociation and FND, this is often neglected for consideration in theoretical models but could account for many facets of the illness. This includes influences on executive control and a diverse range of predisposing factors in FND, which could lead to elevated dissociation and could account for previous findings of alexithymia and neurobiological findings in FND. Throughout this thesis, dissociation has been found to correlate with psychological measures, have a particular influence on some subtypes of FND, and have a relationship with neurobiological findings from EEG and inflammation studies.

8.2.1 Psychological Correlates of Dissociation

Chapter 5 mainly explored the psychological correlates of FND and explored these in relation to dissociation. The study identified that dissociation was elevated in FND and that this correlated negatively with Anhedonia, Cognitive Flexibility, Hopefulness, Rumination, Resilience, and Social Support and positively with Anxiety, Stress, Depression, and social isolation. The identification of elevated dissociation underscores its significance as a central feature of FND. Dissociation has been implicated in various symptoms associated with FND, including motor and sensory disturbances (Campbell et al., 2023; Pick et al., 2020). The findings here further support notions of the role of dissociation in FND and elucidate its relationship with other psychological variables for a deeper understanding of the complex interplay between psychological factors and FND symptomology. Negative correlations between dissociation with both anhedonia and cognitive flexibility suggest that individuals with higher levels of dissociation may experience difficulties in experiencing pleasure and adapting to changing circumstances. This aligns with previous research, highlighting deficits in reward processing and cognitive flexibility in FND (Demartini et al., 2014). Further exploration of these linking mechanisms could support targeted treatments that improve emotional and cognitive functioning.

The research outcomes indicate that it is crucial to examine the impact of dissociation on the well-being of individuals with FND. In Chapter 5, it is demonstrated that dissociation is positively correlated with anxiety, stress, and depression in FND, underscoring its significant role in the mental health and overall well-being of those with the disorder. Moreover, previous studies have linked dissociation to heightened psychological distress and unfavourable

treatment outcomes in other conditions (Lyssenko et al., 2018). Therefore, comprehending the interconnected relationship between dissociation and psychological symptoms is essential for improving the understanding of FND and ameliorating its treatment outcomes. Although the study could be criticised for not including all types of Functional Neurological Disorders (FNDs), it did investigate dissociation in particular subtypes of FND (in Chapter 6), and the extensive sample size allowed for a varied sample to be examined within this study. Previously, mental health and well-being have been explored nearly exclusively as being a product of adverse life events and experiences. Whilst these previous findings must not be overlooked, the role of dissociation should be further examined in FND. Elevated dissociation in the current study was found to be a strong predictor of higher levels of disability, and this could reflect generally higher levels of disability and impairment as a result of dissociation. Of course, this research cannot determine cause and effect, and as such, considerations should include exploration as to whether dissociation is a symptom of other underlying factors.

Negative correlations were identified between dissociation and resilience, hopefulness and social support. These findings underscore the importance of coping resources and social connections in mitigating the impact of dissociation on psychological well-being and in considering broader influences that could lead to increased social isolation. Resilience scores were the lowest in those with FND, and whilst the reason for these results can only be speculated, resilience has previously been linked to other psychological correlates of FND, including alexithymia (Jalilianhasanpour et al., 2018). This could be a product of dealing with increased stress and the unknown in FND (Canna & Seligman, 2020; Kozlowska et al., 2023), including chaotic and unpredictable life changes and reductions in quality of life (which were identified in Chapter 6). Enhancing resilience, fostering hope and strengthening social support networks may serve as protective factors against the adverse effects of dissociation and implicated psychological factors in FND (Herbert et al., 2014). However, the role of social support is often overlooked in FND (Foley et al., 2024), and indeed, some are advised against social support groups and interaction with other patients with the condition for fear that it will "worsen" symptoms. Furthermore, some social isolation and reduced social support may be a product of stigma and reduced care provisions, in addition to chaotic illness narratives and changes in quality of life. Socio-political influences have greatly influenced understandings of FND, and definitions and medical stigma remain a significant influence, lending to adverse views of patients with the condition. Studies have shown that within healthcare, generally, negative attitudes towards FND exist and that there is continued skepticism about the

legitimacy of FND (Barnett et al., 2022; Begley et al., 2023; Evans & Evans, 2010; Kanaan et al., 2011; Marotta et al., 2021; Tinazzi et al., 2022). Not only do these negative attitudes contribute to a lack of research and limited formal training (de Liège et al., 2022; Stone et al., 2020), but they also contribute toward clinical decision-making and in shaping the general population's views of the disorder. Both implicit and explicit attitudes have a direct impact on the care and psychological well-being of individuals who have been diagnosed with functional neurological disorder (FND). Consequently, it is crucial to develop treatment plans to improve patients' well-being, strengthen their support networks and address the broader mindset and treatment of FND.

8.2.3 Dissociation and Neurobiological/Neurochemical Correlates

Elevated dissociation was noted as influencing neurobiological and neurochemical studies within this thesis. Dissociation was found to have a relationship with other neuropsychological constructs (including mood, social support or isolation and quality of life) in Chapter 5, as well as cognitive flexibility. Psychological constructs like these correlate with Dissociation and are associated with brain function and neuroendocrinology (Cacioppo et al., 2015; Lieberz et al., 2021). Thus, relationships between dissociation and altered brain activity or inflammation findings are not linear. Dissociation was found to mediate and correlate with inflammatory markers and resting-state brain activity in this study (Chapter 7). Specifically, correlations were more strongly identified between dissociation and CRP and both frontocentral, centroparietal regions and areas of the SMA. Indeed, previous research has found that dissociation is related to cingulate cortex cortical thickness (Perez et al., 2018), right lateral occipital cortical thickness (Labate et al., 2012) and general functional connectivity in those with functional seizures, particularly in resting state networks associated with the frontoparietal, executive, sensorimotor and default mode networks (van der Kruijs et al., 2012). Previous EEG findings have noted that connectivity and emotion regulation are also associated with dissociation in FND (Kienle et al., 2018). The current thesis adds to these findings and notes that dissociation correlates with specific components in specific frequency bands in resting state data in FND, which displays distinct patterns compared to healthy controls.

To build on emerging neurophysiological research in FND, the current thesis has integrated EEG resting-state data with dissociation measures to explore the neural

underpinnings of FND. Findings demonstrated altered oscillatory activity in key frequency bands, particularly in the beta and gamma ranges, in individuals with FND compared to healthy controls. Specifically, reduced beta-band power was observed in frontocentral and centroparietal regions, aligning with previous studies suggesting disruptions in sensorimotor and attentional networks (Barzegaran et al., 2016; Xue et al., 2013). Heightened gamma-band spectral power in the left parietal region and reduced gamma-band activity in the right temporal region further point to hemispheric asymmetries, which may reflect compensatory mechanisms or disrupted network integrity in FND (Umesh et al., 2017). Moreover, dissociation scores correlated significantly with altered oscillatory activity, particularly in frontocentral regions and the supplementary motor area (SMA), suggesting a direct link between dissociative experiences and functional network disruptions in FND. This aligns with prior neuroimaging studies indicating structural and functional connectivity differences in dissociation, including reduced cortical thickness in the cingulate cortex (Perez et al., 2018) and altered connectivity in frontoparietal, executive control, and default mode networks (van der Kruijs et al., 2012; 2014). The current thesis expands upon these findings by showing that dissociation correlates with neural activity in FND and influences electrophysiological signatures, reinforcing its role as a core feature in the condition.

These findings suggest that oscillatory abnormalities in FND may reflect altered sensory processing, attention, and motor control, with dissociation playing a key modulatory role. The observed reductions in beta-band power and alterations in gamma activity may also have implications for neural inhibition and integration processes, supporting models of disrupted top-down regulation in FND (Edwards et al., 2012). Future research should explore whether these EEG signatures could be leveraged as potential biomarkers for dissociative subtypes of FND and whether they hold predictive value for treatment response or symptom severity.

Taken together, findings suggest that dissociation may play a specific role in brain structure and function but should also be considered in terms of its complex relationship to other neuropsychological, social, and environmental factors. Moreover, dissociation could account for slump-crash reactions seen in FND, the types of symptoms seen, and the variability across the FND population in symptom display through its association with neural connectivity. These results suggest that dissociation may be a crucial factor to consider when studying the neurobiology and neurochemistry of FND. Furthermore, relationships between cognitive flexibility and dissociation emphasise the need to consider its implications in research and treatment practice.

8.3 Subtypes of FND

Symptoms of FND are often listed and described as if they were unrelated to one another and occur at random. However, theoretical models presume that there is an underlying mechanism which somehow shifts to present different symptoms and variations of symptoms within this patient group. In clinical practice and community work, there are reports of symptom clusters occurring consistently and in relation to the predisposing (or triggering) event. For example, those who report a physical event at the onset of the development of FND seem to show correlates with subsequent symptomology, i.e. painful limb injuries are reported commonly prior to the onset of FND and the same limbs are affected in functional dystonia (van Rooijen et al., 2011). Panic attacks, events of emotive significance and events which induce dissociation are commonly reported prior to the onset of functional seizures (Goldstein & Mellers, 2019). This thesis sought to explore these suggested relationships and identified if, statistically, i) symptom clusters could support the identification of distinct and statistically driven subtypes of FND, ii) if there was a relationship between these clusters and additional (non-core) symptoms, and iii) if precipitating events predicted these.

These findings were sought by applying novel statistical techniques such as LCA and LTA, providing a unique opportunity to explore potential subtypes within FND (Collins & Lanza, 2010; Nylund et al., 2007). These methods allowed for the elucidation of underlying patterns of symptomology and the identification of distinct latent classes which represent and are characterised by specific clusters of symptoms (Lanza & Rhoades, 2013; Nagin, 2005). A 7-class solution was identified and suggested that at least seven subtypes of FND may be present, though further research is needed to validate and confirm these findings. Nonetheless, this complexity in the manifestation of symptoms resonates with the principles of chaos theory, which posits that complex systems, such as human behaviour and neurological disorders, can exhibit nonlinear dynamics and sensitive dependence on initial conditions (Gleick, 1987; Strogatz, 2018). In the context of FND, identifying multiple latent classes suggests a dynamic interplay of various factors contributing to symptom expression akin to the intricate dynamics observed in chaotic systems. The inclusion of LTA as an extension of LCA facilitated the exploration of the transition of symptom states (Collins & Lanza, 2010) about additional "non-core" symptoms, including pain and fatigue, suggesting additional symptoms which should be included in the context of FND symptomology. Further explorations posited that the triggering

or precipitating event influenced subsequent subtype predictions. Previous research has noted that symptom profiles of FND can change over time and that symptoms can replace others or that those with FND may present with more than one subtype of FND (Bulter et al., 2021; Nicholds et al., 2022). This temporal instability echoes the "butterfly effect" concept in chaos theory, where small perturbations in the system's initial conditions can lead to significant changes in its subsequent behaviour (Lorenz, 1963) or, in this case, symptom outcomes. By embracing the principles of chaos theory, this study offers a novel perspective on the complexity and dynamism inherent in FND symptomatology, highlighting the need for holistic and dynamic approaches to its assessment and management.

8.3.2 Presence of Dissociation in Subtypes

Dissociation was found not only to predict mental well-being in FND and underpin some of the neurobiological mechanisms in FND but also to play an influential role in predicting symptom clusters or subtypes of FND. The findings of Chapter 6 allude to an intricate relationship between dissociation and subtypes of FND. Specifically, the results reveal that dissociation scores exerted a probabilistically strong influence on specific FND subtypes, notably Class 1 (motor dissociation states), Class 4 (Occasional Neuropathic), Class 5 (Mixed multisystem symptoms), and Class 6 (intermittent seizure subtypes). Moreover, examining the relationship between symptom clusters and precipitating factors in FND, alongside investigations into characteristics such as dissociation, underscores the multifaceted nature of the disorder and its susceptibility to nonlinear interactions (Stone et al., 2019). The results also underscore the pivotal role of dissociation in shaping the heterogenous symptomology observed in FND, aligning with previous literature which has highlighted the significance of dissociation in the disorder (Aybek et al., 2015; Campbell et al., 2023; Cromer et al., 2006; Fobian & Eliott, 2018; van der Bergh et al., 2017; van der Kruijs et al., 2012).

The observed associations between dissociation and specific FND subtypes resonate with principles from chaos theory, which posits that complex systems exhibit nonlinear dynamics and sensitive dependence on initial conditions (Gleick, 1987; Strogatz, 2018). In the context of FND, identifying distinct subtypes characterised by differential associations with dissociation underscores the dynamic and complex nature of the disorder. Analogous to the "butterfly effect" in chaos theory, subtle variations in initial conditions, such as the presence of

dissociative symptoms, may lead to significant variations in symptom expression and clinical outcomes across different FND subtypes. Findings in this thesis between associations of dissociation and FND subtypes also contribute to our understanding of the broader neurobiological mechanisms underlying the disorder, particularly in the context of allostatic load. Previous research has demonstrated links between dissociation and the dysregulation of inflammatory markers not specifically to FND (Hori et al., 2019; Quinones et al., 2020; Powers et al., 2019) and in alterations in brain function and connectivity patterns generally (Krause-Utz et al., 2017; Frewen et al., 2006; Lebois et al., 2021; Lotfinia et al., 2020) and in FND (Pick et al., 2020; Perez et al., 2021; Puentes et al., 2023; Voon et al., 2016). The findings from the current study support this notion, and taken together, findings suggest that dissociation may contribute to an increased allostatic load, defined as the cumulative physiological burden resulting from chronic biological and psychological stress, adversity and assault (McEwen & Ginaros, 2010). Dysregulated inflammatory processes, characterised by elevated levels of inflammatory cytokines such as interleukin-6 (IL-6) and C-reactive protein (CRP), are associated with increased symptom severity and could explain chronicity and slump-crash reactions in FND. Furthermore, alterations in brain function, including aberrant activity in regions of emotion regulation, self-awareness, SMA and salience networks, have been observed throughout the literature. Data in the current study supports the notion that frequency band resting state data and some electrode clusters may also show altered connectivity in specific frequency bands in resting state data. These may also be influenced by dissociation. FND should be viewed, therefore, as a product of embodied brain dysfunction in which multifaceted systems interact to produce the symptom profiles observed and the unique nature of FND symptoms. Furthermore, the current study adds to a growing body of literature highlighting the role of allostatic load in the pathophysiology of the disorder with limitations for the development of future growth of this knowledge and perhaps the development of targeted interventions which are aimed at mitigating adverse effects of dysregulated systems in FND.

8.4 Electroencephalography findings

Despite the early inception of electroencephalography (EEG), the methodology has not received commensurate attention in FND research. This disparity may be attributed to the delayed emergence of neuroimaging technologies in FND coupled with prevailing preferences

for fMRI and BOLD contrast among other newer neuroimaging technologies. However, EEG can offer insights into dynamic brain and electrical activity, complementing data from hemodynamic measures. Whilst EEG has previously been used as a tool to differentiate Functional Seizures from epilepsy (Popkirov et al., 2017) and the use of the Bereitschaftspotential to diagnostic Functional Movement Disorder subtypes (Tomsen et al., 2020), these underpin assumptions of FND as an exclusionary diagnosis. The current thesis explores if EEG could be utilised beyond this to provide information about brain activity and neural networks by investigating the exocellular activity of postsynaptic neurons and pyramidal cells.

Recent studies demonstrate that brain oscillations reflect mechanisms of cerebral integration across several functional domains (Arikan et al., 2021; Frauscher et al., 2015), measured using EEG. Various frequency bands (such as alpha, beta, gamma, delta, and theta) can be explored to provide valuable insight into distinct cognitive processes and brain states, understand neural mechanisms, and identify abnormalities or patterns of activity. Briefly, higher-frequency bands in EEG (alpha, beta, gamma) are associated with processes associated with higher-order cognitive function, including those of theoretical importance to FND (Knyazev, 2017). For example, alpha oscillations have been implicated in attentional processes, while beta oscillations are associated with motor control and executive functions (Putman et al., 2014; Schmidt et al., 2019). Gamma oscillations are often observed during cognitive integration tasks, but there remains much debate over their functions (Buzsáki & Wang, 2012; Herrmann & Demiralp, 2005). Lower frequency bands (delta, theta) are associated with more primitive mechanisms, including attention, drowsiness, memory, movement, learning, emotion regulation and spatial navigation, as well as the maintenance of bodily functions (Buzsáki & da Silva, 2012; Frauscher et al., 2015).

The current thesis did identify differences in frequency bands in FND in an adult mixed-symptom population. Frequency bands implicated were reduced alpha activity (specifically in frontocentral, centroparietal and temporal sites), reduced beta activity in centroparietal regions and reduced gamma in temporal regions. Previous research into children with FND found excessive theta and delta power in electrode clusters that corresponded to posterior rather than frontal regions (Kozlowska et al., 2018). Differences between the current findings and previous research could indicate differences in the neurobiology of FND between children and adult samples, and previous research does note that symptoms display differently between these two populations (Vassiopoulos et al., 2022; Yong et al., 2023). Other research has noted that there

are also alterations in frontal and central regions in children with FND using ICA data-driven approaches (Rai et al., 2022), which supports the findings of the current study. Findings support notions of altered connectivity in different frequency bands in FND. Further investigations to elucidate the precise mechanisms of the observed differences and their implications for the diagnosis and management of both paediatric and adult populations are, however, needed. This is an exploration of potential differences in subtypes of FND.

Further explorations aimed to explore the potential different frequency bands in areas associated with the salience network, temporal parietal region, SMA, DMN and parts of the DMN. Previous research using EEG in children and adolescents with FND has found increased automatic and cortical arousal and increased activation of nodes of the Default Mode Network (DMN), salience network (dorsal ACC/dorsomedial PFC), and supplementary motor area (SMA) in resting state studies (Kozlowska et al., 2018; Radmanesh et al., 2020). This may differ between subtypes. For example, in functional seizure subtypes, previous research has found decreased gamma synchronisation between frontal and posterior regions (Xue et al., 2013), decreased functional connectivity in widespread critical regions in the alpha band (Barzegaran et al., 2016) and heightened gamma-band spectral power in the left parietal region with lower gamma band spectral power in the right temporal region (Umesh et al., 2017). A recent study found that both beta and gamma oscillations were higher in those with functional seizures than in an epilepsy control group (Rai et al., 2022). The current study employed a mixed FND subtype group, and findings cannot be attributed to specific subtypes of symptoms. However, this requires further exploration, and the findings here could instead be attributed to underpinning neural mechanisms that operate among all subtypes of FND.

The findings presented in this thesis support the notion that there are differences in frequency oscillations in different clusters of electrodes. By applying theoretically driven approaches based on topographical maps (Giacometti et al., 2014) and by applying procedures akin to those in previous research in this area, which explored EEG analysis of DMN in a paediatric sample of FND (Kozlowska et al., 2018) the study aimed to be able to explore direct comparisons to previous work. In particular, increased activity was noted in delta in electrode clusters representing the DMN, SMA and Temporal regions. Reduced activity in FND was noted in clusters presenting the Salience network (Alpha), SMA (Alpha, Beta and Gamma) and the Temporal region (Beta and Gamma). In further explorations of the component parts of the DMN, reduced activity was noted in the PCC (Delta and Alpha), Precuneus (Delta and Alpha) and vmPFC (Delta, Alpha and Gamma) in FND. Some of these findings are also related to

inflammatory markers and dissociation, further elucidating the role of bidirectional mechanisms underpinning FND. In these more exploratory investigations, it is essential to note that whilst findings indicate differences, information about these subcortical regions is based on the inference of scalp recordings. More accurate means of determining underlying areas of difference are needed. The limitations of this approach are discussed at length in the limitations section of this chapter.

8.5 Inflammation

Within this thesis, a further key finding relates to the role of inflammation. In chapter 7, individuals with FND exhibited higher levels of inflammation when measured by IL-6 and CRP compared to healthy-matched controls. The study highlights that specific inflammatory markers are likely to play a significant role in the relationship between FND and neural networks and dissociation. Previous studies in this field have focused mainly on cortisol. However, these studies have produced mixed results due to the inconsistent methods employed (Apazoglou et al., 2017; Bakvis et al., 2009; Chung et al., 2023; Weber et al., 2024). Although cortisol is essential, it is not a cytokine with specificity. Therefore, the findings presented in this study, which utilise more widely recognised and stable trait markers of inflammation (IL-6 and CRP), contribute to the existing literature and support considering these markers and the role of neuroinflammation in FND.

Higher levels of inflammation persist even when considering covariates like depression, anxiety, stress, and BMI in the IL-6 model. However, CRP is mainly influenced by physiological measures such as BMI and psychological measures, especially depression and dissociation. It is widely acknowledged that inflammation and cytokine concentration can impact many physiological and psychological processes (Becher et al., 2017; Levin & Godukhin, 2017; McAfoose & Baune, 2009; McKim et al., 2016; Osipova et al., 2018). Several factors influence IL-6 and CRP, including psychological stress and physical activity (Petersen & Pedersen, 2005). While IL-6 initiates the inflammatory cascade, CRP is a downstream marker of inflammation and is often considered a systemic inflammation marker (Pepys & Hirschfield, 2003). Depression has consistently been associated with immune system function changes and increased inflammation (Miller et al., 2009). Chronic stress and depressive symptoms can dysregulate the HPA axis and nervous system, leading to increased production of pro-inflammatory cytokines, such as IL-6. Furthermore, depression is linked to changes in

health behaviours (poor diet, physical inactivity) and physiological factors (dysregulated cortisol) that can further exacerbate inflammation (Miller, 2009).

CRP, a downstream marker of inflammation, may be particularly sensitive to the effects of depression due to its direct association with IL-6 production. Unlike IL-6, CRP production is influenced by multiple factors, including genetic predisposition, environmental factors, and chronic diseases (Khera et al., 2005). Studies have demonstrated that depression can directly affect CRP levels through its impact on hepatic function, insulin resistance, and adiposity (Howren et al., 2009). Additionally, depression-related behaviours such as poor sleep quality and substance abuse may contribute to increased CRP production independently of IL-6 levels (Howren et al., 2009). It is important to note that the findings do not undermine the role of inflammation in FND. Instead, reduced activity caused by mobility impairments, fatigue or overlap of symptoms that lead to decreased quality of life and depression could explain increases in CRP and the mediation between CRP and depression in FND. The persistence of elevated IL-6 levels, even when accounting for covariates, underscores its robustness as a biomarker and suggests a pivotal role of chronic inflammation in the pathogenesis of FND. However, it is essential to consider how these may relate to inflammatory pathways, and exploring other molecules is essential for advancing understanding in this domain.

The results of this thesis showed a correlation between dissociation and both IL-6 and CRP in FND but not in healthy controls. This is likely because extreme levels of dissociation were reported in the FND group, whereas the healthy controls mainly reported baseline levels of dissociation. These findings suggest that dissociation is a crucial aspect of FND symptomology. Additionally, dissociation may affect inflammation levels in FND, which could be related to the principles of allostasis (McEwen, 2003). This implies that individuals with FND may have dysfunctions that have detrimental effects on allostatic load, subsequently affecting other systems and contributing to further dysfunctions (Grassi-Oliveira et al., 2008; Lamb et al., 2021; Staniloiu et al., 2010). Dissociation is believed to be a psychobiological response to allostatic load, and previous research has linked high levels of IL-6, CRP, and lower cortisol in FND (Keynejad et al., 2019). Therefore, theoretical models of FND should consider systemic and chronic inflammation, and further research is needed to explore the relationship between dissociation and inflammation in FND.

The current thesis extends prior work by examining the interaction between inflammatory markers and EEG activity. This further analysis elucidated the role of

inflammation in neural activity, particularly within some regions of interest in FND, highlighting the potential neuroimmune contributions to FND pathophysiology. Significant correlations were found between IL-6 and CRP levels and alterations in EEG spectral power, particularly in frontocentral and sensorimotor regions. Specifically, higher IL-6 levels were associated with increased gamma-band activity in the supplementary motor area (SMA) and reduced beta-band power in centroparietal regions, suggesting a link between neuroinflammatory processes and disrupted motor control networks. These findings align with existing literature, which shows that pro-inflammatory cytokines influence neural excitability and oscillatory activity, potentially through mechanisms involving microglial activation and glutamatergic dysregulation (Drevets et al., 2008; Felger & Treadway, 2017). Moreover, the interplay between dissociation, inflammation, and EEG abnormalities further complicates the linear interpretation of these findings. Dissociation scores correlated with both inflammatory markers and altered oscillatory patterns, reinforcing its role as a modulator of neurobiological dysfunction in FND. Combined, the findings indicate that inflammation may mediate neural network dysfunction in FND and further reflect a system in which allostatic load has increased, affecting emotional arousal and reducing neural activity.

Some measures of inflammation were more related to neural activity than others or more influenced by combinations of dissociation and depression. Thus, they demonstrate the complex interplay between these specific mechanisms and the activation of immune and inflammatory cells in response to changes in neuroplasticity and brain networks, as well as the influence of measures of distress and dissociation. Notably, CRP levels showed stronger correlations with EEG activity in frontoparietal and sensorimotor regions, a pattern consistent with research indicating that elevated systemic inflammation may contribute to aberrant connectivity in resting-state networks (Harrison et al., 2015; Menon, 2011). This supports the hypothesis that neuroimmune dysregulation could drive, or at least exacerbate, the functional neural alterations observed in FND. The bidirectional nature of the relationships between dissociation, inflammation, and EEG alterations presents a complex challenge in understanding causality. While heightened inflammation may disrupt neural oscillatory stability, it is equally plausible that persistent neural dysregulation contributes to prolonged inflammatory responses via dysregulated autonomic and hypothalamic-pituitary-adrenal (HPA) axis activity. Given this interplay, future research should employ longitudinal designs to assess whether inflammation precedes EEG alterations or vice versa, as well as whether these factors predict symptom progression or treatment response in FND. In essence, all of these states may act cyclically,

resulting in cascades of dysfunction across these symptoms, wherein one becomes a response to dysfunction in another.

8.6 An embodied brain model of FND

The findings throughout this thesis demonstrate that the conceptualisation of FND should go beyond that of a neural network disorder and that FND should be considered as a "whole body" or embodied brain disorder. Previous research demonstrates that biological markers and bodily dysfunctions could underpin neural network dysfunction in FND (Asadi-Pooya, 2016; Milano et al., 2023; Villagrán et al., 2021). The current study adds to this argument further and considers that psychological states like dissociation and biological dysfunction, including inflammation, underpin neural network dysfunction in FND. Whilst, of course, these findings cannot state cause and effect, they do emphasise the essential need to note relationships between dissociation, other psychological facets, neuroinflammation and neural dysconnectivity in FND. FND could be considered a product of dysfunction in neuroinflammation, wherein chronic inflammation has led to impaired neural networks. They also elucidate the role of dissociation within this relationship and the role of subtypes in FND. Breaking the bidirectional cycle in which these constructs operate could lead to significant changes in quality of life, psychological distress and symptom reduction.

As such, the current thesis tentatively proposes a model of FND that incorporates these findings and can be expanded upon further with future research. This model is displayed in Figure 5 and discussed below.

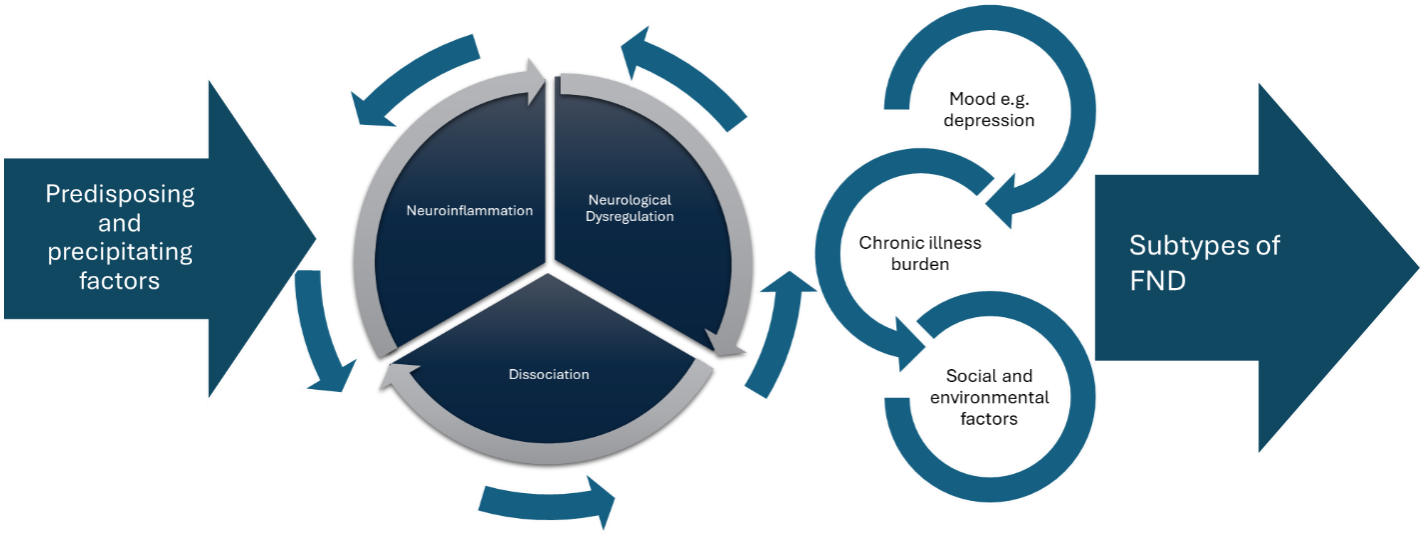

Figure 5: Proposed Embodied Brain Model of FND

The proposed model conceptualises FND as a complex, bidirectional interplay between neuroinflammation/chronic inflammation, neural dysregulation, and dissociation. All of these are influenced by predisposing and precipitating factors and maintained by broader psychological, social, and environmental factors, which can feed into the cycle or dysregulate symptoms. Finally, the model proposes that levels and influence from the middle parts of the model lend to the development of various subtypes of FND.

Previous literature has extensively documented predisposing (e.g. genetic, early-life adversity, personality traits) and precipitating (e.g., viral infections, surgeries, psychological stressors) factors in the development of FND (Pick et al., 2020; Nicholson et al., 2020). My PhD findings directly contribute to this area by identifying specific triggers that significantly predict symptom clusters, including viral infections, head injury, and operations/surgery, as well as cases where no identifiable trigger was present. This latter finding underscores the heterogeneity of FND onset. It suggests that while identifiable external events may initiate symptoms for some, others may develop symptoms through endogenous mechanisms (e.g. pre-existing neurobiological vulnerability, prior dissociative tendencies or inflammatory states) or by complex multiple factors which are not easily pinpointed to one direct, specific event.

A major contribution of this thesis is the integration of inflammation as a core component of FND pathophysiology. My research demonstrated inflammatory markers (IL-6 and CRP) in FND. Acute pathways of neuroinflammation (as denoted by CRP findings) may also be influenced by enforced life changes, emotional dysregulation or mood as a byproduct of

reduced function, cognitive flexibility or predisposing events of emotional valence. CRP and mood, particularly depression, may also lend to elevated dissociation or be a result of elevated dissociation and subsequent symptomology. Though CRP was influenced by mood and dissociation, IL-6 levels remained elevated independent of mood, BMI, or mediation use, indicating that systemic inflammation contributes to neural dysfunction in this disorder. This may contribute to neural dysregulation and alterations in brain function, ultimately leading to the manifestation of FND symptoms. Additionally, my EEG findings highlight functional brain alterations in FND, including dysregulated activity in the supplementary motor area (SMA) and frontoparietal networks, which have previously been implicated in sensorimotor integration, self-agency and dissociation (Perez et al., 2018; Kienle et al., 2018). The findings from the current thesis align with prior research suggesting that neural network dysfunction plays a key role in FND symptoms. However, my study adds novel evidence by demonstrating that dissociation correlates with both inflammation and EEG alterations, reinforcing the idea that dissociation is not purely a psychological construct and has neurobiological underpinnings.

The proposed model here explicitly frames dissociation as both a cause and a consequence of FND symptoms. Chronic dissociation may contribute to neural network instability, impairing the ability to regulate sensorimotor processes. Simultaneously, neural dysregulation (which can be driven by inflammatory pathways) may also increase dissociative symptoms, reinforcing a maladaptive feedback loop. This bidirectional relationship is a critical expansion upon previous models, which often position dissociation as a purely psychological phenomenon and only as a predisposing factor, without acknowledging its biological dimensions and the negative cycle created by these three constructs.

While mood disorders, chronic illness burden, and social/environmental stresses were not always directly implicated in the casual pathways of FND in this set of studies, they were considered influential in maintaining or exacerbating symptoms. Depression and anxiety, for instance, in some studies are highly comorbid with FNS (Brown & Reuber, 2016) and could contribute to neuroinflammatory activity and neural dysregulation, thereby sustaining or amplifying FND symptoms over time and acting as a trigger for ‘crash-slump’ reactions. Likewise, individuals with chronic illness often experience heightened allostatic load, which may exacerbate neuroinflammation and dissociative processes (McEwen, 2003; Keynejad et al., 2019). The inclusion of chronic illness burden and environmental and social factors in the model reflects their role in maintaining the cycle rather than directly initiating it. This

distinction is important in differentiating the primary mechanisms of FND pathogenesis from secondary factors that could contribute to its persistence. Further work in this field is needed.

A final key contribution of this PhD research was the empirical identification of at least seven distinct FND subtypes, each with unique symptom clusters. This supports the notion that FND is not a monolithic disorder but a spectrum condition with multiple distinct pathways. The findings from latent class analysis (Chapter 6) reinforce that different subtypes may arise from different interactions of the core mechanisms within the model, explaining the diverse symptom presentations observed in clinical settings. For example, my research suggests subtypes with prominent dissociative features may be more biologically linked to inflammatory and neural network dysfunctions. In contrast, subtypes with more substantial sensorimotor involvement may have different underlying disruptions in the brain's predictive processing or movement regulation areas on a functional level. These insights contribute to the growing movement to redefine FND classification based on symptom clusters rather than singular diagnostic labels.

To illustrate the complexities further of FND-specific mechanisms from general chronic illness effects, consider the example of functional seizures. If this thesis had focused solely on functional seizures, an obvious LTD comparison group would have been epilepsy patients. However, even within epilepsy, seizure types vary significantly, and functional seizures can often present alongside epileptic seizures, making it difficult to establish a clean one-to-one comparison. The same challenge applies to broader FND research, where heterogeneous symptoms, comorbidities, and overlapping pathophysiological and biopsychosocial mechanisms complicate interpretation. Thus, while boldly included in the thesis, this model does not propose a singular explanatory mechanism for all cases of FND. Instead, it offers a flexible, multidimensional framework for understanding how different biopsychosocial influences interact to shape individual presentations of FND. It also serves as a reminder that FND goes beyond a brain network dysfunction; it is a disorder of ‘embodied brain’ combining findings of body, brain and mind, as well as environmental, social and mood, in a single framework.

The model remains preliminary and requires much more empirical validation. However, it provides a valuable framework for conceptualising the interplay between inflammation, neural dysregulation, and dissociation in FND. Future research should validate the proposed interactions through longitudinal studies examining whether dissociation, inflammation and

neural dysfunction predict symptom progression (or relapse). Further multimodal neuroimaging and biomarker analysis could help to refine our understanding of how neural networks and inflammation interact with FND subtypes. Interesting future progression for the development of understanding of subtypes could consider stratifying FND patients by latent symptom clusters to determine whether specific pathways (e.g., inflammatory, dissociative, sensorimotor) are more relevant to certain subtypes experimentally. This, in turn, could enable the exploration of interventions which target these mechanisms, for example, whether anti-inflammatory treatments or neural network modulation therapies could be used to reduce dissociation or improve motor symptoms in FND.

8.7 Limitations

This thesis and the studies contained within are not without their limitations. While these have mainly been addressed throughout, some general considerations and more specific points about the multimodal nature of the research need to be addressed further.

8.7.1 Exploratory Nature of Subtype Identification

Whilst seven subclasses were statistically and successfully identified within the literature, this should be considered an exploratory study, and there is undoubtedly more work which could be done to enhance and refine the study's findings further. In an examination of the scale items, for example, there may have been missed opportunities to consider further distinct seizure subtypes or distinct functional cognitive subtypes, which are increasingly being noted throughout the literature (e.g., Ball et al., 2020; McWhirter et al., 2020; Teodoro et al., 2018). Thus, further exploration and improvements to this scale would be advantageous. Furthermore, the incorporation of Exploratory Factor Analysis (EFA) followed by K-means clustering (EKA) alongside Latent Class Analysis (LCA) could have provided complementary insights into the latent structure of the observed variables. While LCA identifies latent classes based on observed response patterns, EFA explores underlying factor structures and identifies latent dimensions that contribute to the observed variance (Fabrigar et al., 1999) and allows for

the exploration of relationships between variables by identifying shared variance. Integrating these exploratory techniques with LCA enhances the validity and robustness of the identified classes, offering a more comprehensive exploration of the latent structure of the data (Lubke & Neale, 2006). Additional statistical analysis like EFA, EFK and scale validation would provide a more nuanced understanding of the underlying dimensions shaping class membership and corroborate and validate the findings through distinct exploration of factor patterns and scale validation (Marsh et al., 2009).

8.7.2 Methodological Considerations in Biomarker Analysis

Within the experimental study in Chapter 7, inflammation manufacturers used ELISA assays, which are sensitive and widely used in quantifying protein concentrations. However, they may have limitations in specificity as cross-reactivity with other proteins or interference of biological samples can affect the accuracy of the measurements. Care was taken to ensure that batch-to-batch variability was reduced, and sample handling procedures were rigorous. Standardised assay protocols were followed throughout. However, alternative assay techniques, including multiplex immunoassays or mass spectrometry-based approaches, should be considered to validate the findings and explore distributions between different markers, which were not considered here. Additionally, immunohistochemistry should be applied to investigate molecular pathways and cellular processes associated with alterations in inflammatory markers and identify different inflammation pathways that may be present.

8.7.3 Sample Size Considerations in Inflammatory Studies

A further key limitation in biomarker research, particularly in neuroinflammatory studies, is the sample size required to detect robust effects. Studies investigating inflammatory markers such as IL-6 and CRP typically require large cohorts to account for variability in immune function, given the influence of biological, environmental and psychological factors on cytokine levels (Dhabhar, 2014; Lambregts et al., 2023). Many large-scale inflammatory studies rely on hundreds or even thousands of participants to ensure adequate statistical power and generalisability (Marsland et al., 2017).

In this thesis, funding constraints and the multimodal nature of the study (including assessment of inflammation alongside EEG and dissociation analyses) limited the sample size available for phlebotomy-based biomarker collection. However, despite this limitation, significant relationships between inflammation, dissociation and EEG activity were still observed, suggesting that the observed effects are meaningful and not merely statistical artifacts. Additionally, the use of matched healthy controls, alongside rigorous statistical adjustments for BMI, mood, and medication use, helped account for potential confounding factors and increase the reliability of inflammatory findings despite the smaller sample size. Nonetheless, future research should aim to replicate and expand on these findings in larger cohorts, integrating EEG, inflammatory markers, and key neuropsychological constructs to validate the associations identified in this study further. The present findings contribute valuable preliminary evidence that neuroimmune dysfunction and dissociation may play a role in the pathophysiology of FND, warranting further exploration with larger, multimodal datasets.

8.7.4 Limitations in EEG Analysis and Neural Correlates of FND

In relation to EEG data, the approach taken in this study involved quantifying EEG power data for specific regions of interest, particularly those associated with the default mode network (DMN), salience network, and supplementary motor area (SMA). Channel selection was guided by a topographical map developed by Giacometti et al. (2014), which facilitated the identification of clusters of electrodes corresponding to these regions. While topographic mapping techniques are commonly used to infer underlying brain activity from scalp EEG data, it is essential to acknowledge the inherent limitations in the precise localisation of such an approach. Despite this limitation, selecting electrode clusters based on established literature (Giacometti et al., 2014; Kozlowska et al., 2018) aimed to facilitate investigation into the neural correlates of dissociation and inflammation in FND. The channels selected for electrode clusters were chosen to adhere to best practices and ensure transparency in EEG studies (Keil et al., 2014). Due to the complexity and scale of the dataset, as well as conceptual disagreements within the literature, two rounds of electrode clusters were explored. Specifically, areas implicated in the DMN, salience network, and SMA were delineated into clusters according to established literature recommendations (Seeley et al., 2007; Williams, 2017). In the subsequent analysis, more specific elements of the DMN were investigated,

including separate clusters for the posterior DMN, posterior cingulate cortex, precuneus, and temporal lobe. These selections were based on verified topographical maps and cluster suggestions from previous studies (Giacometti et al., 2014; Kozlowska et al., 2018). However, it is essential to note that the precise localisation of neural activity using scalp EEG data may be limited, and further validation of these electrode clusters is warranted. Additionally, while this approach enables the investigation of specific brain regions implicated in FND, the interpretation of results should be cautious, considering the inherent limitations in spatial resolution and the potential for confounding factors. Further research utilising complementary neuroimaging techniques, such as functional magnetic resonance imaging (fMRI), could provide additional insights into the spatial distribution of neural activity and help validate the findings obtained from EEG-based analyses. In addition, other, more advanced forms of EEG analysis, including independent component analysis (ICA).

ICA is a powerful technique for decomposing EEG data into spatially independent components, thereby revealing distinct brain networks or sources of neural activity (Makeig et al., 1997). Despite its utility, ICA was not applied in the present analysis. Incorporating ICA could have facilitated the investigation of brain networks associated with inflammation and dissociation, allowing for the examination of dynamics and interactions among neural networks and providing a more comprehensive understanding of the neural correlates and neurobiological mechanisms underlying FND. Dipole modelling, another valuable technique, was also not utilised in this research. This enables estimation of the location and orientation of electrical sources based on EEG scalp recordings. The absence of dipole modelling in the analysis also raises concerns about the interpretation of findings, particularly regarding subcortical regions such as the vmPFC and the DMN. Therefore, caution should be exercised when interpreting the findings related to these regions. Additionally, advanced EEG processing techniques, such as the application of Spiking Neural Networks (SNNs), warrant consideration in future research endeavours. SNNs offer a biologically plausible framework for exploring differences in connectivity throughout brain data, providing a more nuanced understanding of the complex interactions among neural networks implicated in FND. Whilst the methods employed in the thesis provide valuable insights into the neural correlates of FND and their relationship to inflammatory and neuropsychological facets, notable limitations should be addressed in future research. By incorporating techniques, including ICA, dipole modelling, fMRI, and SNNs, researchers can overcome these limitations and more comprehensively understand the neurobiological underpinnings of FND.

8.7.5 Conceptual Challenges in LTD Control Groups and Representativeness

The use of long-term disability (LTD) control groups throughout the research in this thesis serves a dual function first, to differentiate mechanisms specific to FND from those associated with chronic illness more broadly, and second, to address critiques that FND-related findings may reflect general consequences of chronic ill health rather than disorder-specific features (Kemp et al., 2022; Nicholson et al., 2020). Given that FND shares symptomatic overlap with conditions such as ME/CFS, fibromyalgia, chronic pain and multiple sclerosis (MS), including fatigue, cognitive dysfunction, autonomic dysregulation, and mood disturbances, and LTD comparison group provides a valuable framework for establishing specificity in symptom presentation, psychological correlates, and neurobiological markers (Stone et al., 2020; Pick et al., 2020). However, the interpretation of findings derived from LTD groups is not without methodological and conceptual challenges, which merit careful consideration.

A central challenge in using LTD groups is the heterogeneity of the conditions included. LTD cohorts, especially those in this thesis, encompass a broad range of illnesses, each with distinct underlying pathophysiology, diagnostic criteria, and illness trajectories. While FND is characterised by disrupted functional connectivity and sensorimotor dysfunction (Hallet et al., 2021), many LTD conditions are driven by autoimmune, inflammatory, neurodegenerative, or metabolic processes. This pathophysiological diversity complicates direct comparisons, as differential mechanisms may drive overlapping symptoms. Thus, an elevated level of anxiety and fatigue in an LTD group may have different underlying causes than similar symptoms observed in FND, limiting the interpretability of direct comparisons.

A directly related challenge is that FND frequently coexists with various psychological or medical comorbidities, contributing to the complexity of its clinical presentation. Studies report that anxiety disorder is commonly reported, followed by mood disorders and neurodevelopmental disorders; around 40% of patients with FND have a dual psychological diagnosis (Carle-Toulemonde et al., 2023). Additionally, patients with FND often report other symptoms, including fatigue and cognitive symptoms, and many will have a dual diagnosis with ME/CFS and/or fibromyalgia. This high prevalence of comorbidities underscores the importance of comprehensive approaches to FND, and a symptom-pure group may be near

impossible to obtain or clarify in research, but it further complicates analysis in comparison to LTD groups.

Furthermore, the inclusion criteria for LTD groups vary across studies, leading to inconsistencies in sample composition and representativeness, and they certainly have varied in the current thesis across all studies, too. For example, LTD cohorts often overrepresent certain chronic illnesses (e.g. fibromyalgia, ME/CFS) while underrepresenting others (e.g., degenerative neurological conditions like Parkinson's or Huntington's disease), creating potential biases in symptom profiles (Greenland et al., 1999; Arnold & Ercumen, 2016). Without careful sample stratification, comparisons between FND and TLD groups may be influenced by a disproportionate representation of conditions with shared features, artificially inflating the perceived similarity or difference between groups. Yet, clear guidelines for using LTD groups and which groups to target for best presentiveness have not been produced. Nor is there explicit agreement within the field of FND as to which groups would best serve this purpose.

Another critical issue is selection bias in LTD control groups. Recruitment methods often rely on self-reported diagnoses, which may vary in diagnostic accuracy and rigour across conditions and studies (Althubati, 2016; Tripepi et al., 2010). Given that FND itself is often misdiagnosed or overlooked in clinical practice, the possibility exists that some individuals classified within an LTD group may have undiagnosed functional symptoms, further complicating direct comparisons. Additionally, individuals who volunteer for LTD studies may differ systematically from the broader chronic illness population, as they tend to have higher levels of healthcare engagement, greater symptom severity, or distinct illness perceptions, introducing systematic differences in the control group which may not be reflective of the broader LTD population (Chen et al., 2022; Dahlen & Charu, 2023; Moreno-Fernandez & Matute, 2020).

Even within subtypes of FND, comparison with an LTD group presents distinct methodological challenges. For example, suppose this thesis had focused solely on functional seizures rather than a broader spectrum of FND subtypes. In that case, a logical comparison group might have been individuals with epilepsy, as both conditions involve seizure-like events and potential neural hyperexcitability. However, even this comparison is fraught with complexity, particularly in online sampling contexts where individuals with functional seizures may present with overlapping seizure types or co-occurring neurological conditions (Brown &

Reuber, 2016). Additionally, not all seizures look the same, even within functional or epileptic subtypes, and the variability in the presentation, diagnosis, and comorbidities would complicate direct comparisons between the two groups (LaFrance et al., 2013). This illustrates a broader issue with control group selection in FND research, where heterogeneity in presentation, even with a single symptom domain, renders establishing a "perfect" control group nearly impossible.

In this thesis, several strategies were employed to address these challenges. First, the use of multiple control groups (healthy controls and LTD groups) across different studies allowed for a broader comparative framework, reducing the risk that findings were solely by the inclusion or exclusion of an LTD sample. While an LTD comparison group was not feasible in the EEG and inflammatory marker studies (due to resource constraints), the inclusion of LTD controls in other analyses ensured that key psychological and symptomatic distinctions could still be examined. Further, this thesis explicitly considers which symptoms and correlates may be specific to FND versus those expected in chronic illness populations more broadly. Findings suggesting that elevated dissociation is a unique feature of FND (rather than a general chronic illness correlate) provide evidence that FND-specific mechanisms contribute to symptomatology beyond those expected in chronic illness alone. However, future research should continue refining the use of LTD comparisons, potentially incorporating stratified matching techniques to control for illness duration, disability severity, and psychosocial factors, as well as exploring biomarker-based comparisons to distinguish better shared versus disorder-specific pathophysiological mechanisms. Implementing carefully matched LTD control groups in future studies could ensure balance in illness duration, severity, functional impairment and symptom clusters. Beyond this, future research should also use neurobiological markers (such as EEG, inflammatory markers, and neuroimaging) in LTD comparisons to differentiate FND-specific disruptions from broader chronic illness mechanisms. Finally, the examination of longitudinal trajectories should be undertaken, as chronic illness conditions often exhibit different symptom progressions compared to FND, which fluctuates over time in ways that may not align with progressive or autoimmune disorders.

8.8 Future Research

Considering the limitations discussed in the previous section, the current set of studies represents an initial exploration into many areas of FND. It lends direction to exploration for future research. Concerning the identification of the subclassification of FND, the identification of seven subclasses serves as a starting point for future investigation and refinement. However, it is crucial to recognise that the study is inherently exploratory, and there are ample opportunities for enhancing and refining the findings in future research endeavours. For instance, an in-depth examination of the scale items could unveil missed opportunities to capture distinct seizure subtypes of function cognitive subtypes, which have garnered increasing attention in the literature (Ball et al., 2020; McWhirter et al., 2020; Teodoro et al., 2018). Thus, future studies could benefit from refining the measurement tool to encompass a broader spectrum of FND manifestations. In addition to refining measurement tools and statistical techniques, future research endeavours should also prioritise participant participatory involvement (PPI) to ensure that the subclassification of FND is grounded in the lived experiences and perspectives of individuals affected by the disorder. Engaging participants in the research process, from study design to interpretation of findings, fosters a sense of ownership and empowerment, ultimately enhancing the relevance and applicability of research outcomes to clinical practice and patient care. By embracing a PPI approach, researchers can collaboratively explore the diverse manifestations of FND and develop subclassification frameworks that resonate with the unique needs and experiences of individuals living with the disorder.

Moreover, the incorporation of additional statistical techniques, such as Exploratory Factor Analysis (EFA) followed by K-means clustering (EKA), alongside Latent Class Analysis (LCA), could provide complementary insights into the latent structure of the observed variables. While LCA identifies latent classes based on observed response patterns, EFA explores underlying factor structures and identifies latent dimensions contributing to the observed variance (Fabrigar et al., 1999). Integrating these exploratory techniques with LCA can enhance the validity and robustness of the identified classes, offering a more comprehensive exploration of the latent structure of the data (Lubke & Neale, 2006). Additionally, conducting scale validation procedures would further corroborate and validate the findings by examining factor patterns and ensuring the reliability and validity of the measurement instrument (Marsh et al., 2009). The development and refinement of this

measurement tool should capture a broader range of FND manifestations and integrate further exploratory statistical techniques to enhance the validity of subclassification approaches and ensure the measurement's reliability. Future research in this sphere could support the enhancement of research approaches and have implications for targeted approaches in clinical practice.

Neuroinflammation was confined to IL-6 as CRP levels seemed more moderated by physiological facets (particularly depression and dissociation). Nonetheless, in the current study, neuroinflammation was evidenced by elevated interleukin-6 (IL-6) levels as a significant factor in the pathophysiology of FND. IL-6 is a pro-inflammatory cytokine implicated in various neurological diseases through its role in neuroinflammatory processes and synaptic dysfunction (Erta et al., 2012; Gruol, 2015). Importantly, IL-6 has been shown to exert its effects on neuronal function via epigenetic modifications of Brain-Derived Neurotropic Factor (BDNF), a key regulator of neuronal survival and plasticity (Karpova et al., 2014; Kowiański et al., 2018; Leal et al., 2017; Sleiman et al., 2016). Dysregulation of BDNF signalling pathways could be implicated in the pathogenesis of FND as it is associated with alterations in neuronal excitability and synaptic transmission, which is known to be altered in FND (Aybek et al., 2019; Carlozzi et al., 2016). Therefore, investigating the relationship between IL-6-mediated neuroinflammation and epigenetic modifications of BDNF represents a promising avenue for future research in FND, with potential implications for developing targeted therapeutic inventions aimed at restoring neuroplasticity and mitigating symptom severity. Future research could also explore alternative assay techniques, including multiplex immunoassays or mass spectrometry-based approaches, to validate findings and explore distributions between markers. ELISA assays provide quantitative measurements of IL-6 and CRP levels but not of underlying biological mechanisms driving changes in inflammation. Incorporation of complementary molecular and cellular techniques, including gene expression analysis or immunohistochemistry, could support investigations of the molecular pathways and cellular processes associated with alterations in inflammatory markers in FND.

Conversely, C-reactive protein (CRP), a non-specific acute-phase reactant, lacks specificity for brain-related processes and may be influenced by a myriad of non-brain-involved clinical contributions. In the current thesis, CRP levels were influenced by dissociation and depression, highlighting the role of neuropsychological states in FND but signalling the need for more specific biomarkers, too. BDNF emerges as a potential candidate biomarker which may offer greater specificity than CRP in diagnosing and stratifying

individuals with FND. BDNF, centrally involved in neurodevelopment, synaptic plasticity and neuronal survival, has garnered attention as a putative biomarker based on previous research findings (e.g., Aybek et al., 2021; Chen et al., 2019). Future research should explore the utility of BDNF as a diagnostic marker in FND, with particular emphasis on its specificity and sensitivity in distinguishing FND from other neurological and psychological conditions. Additionally, investigations into the mechanistic underpinnings of BDNF dysregulation in FND, including its interaction with inflammatory pathways and epigenetic modifications, hold promise for elucidating the pathophysiological mechanisms of the disorder and restoring homeostasis to alleviate symptom burden.

In relation to EEG, whilst comprehensive, additional techniques could have been applied to the data to add several critical dimensions to the findings and address some of the present limitations. ICA is a powerful technique for decomposing EEG data into spatially independent components and representing distinct brain networks or sources of neural activity (Makeig et al., 1997), and this was not applied here. Even though only a few channels were used, and higher densities of EEG channels may provide more spatial investigation and the accuracy of ICA decomposition, extracting meaningful components from EEG with a limited number of electrodes is still feasible. This could support the investigation of brain networks associated with inflammation and dissociation and enable the examination of dynamics and interactions to provide a more comprehensive understanding of neural correlates and neurobiological mechanisms. Additionally, dipole modelling was not applied, which could enable the estimation of the location and orientation of electrical sources based on EEG scalp recordings. Findings, particularly of the vmPFC and DMN regions in his study, should, therefore, be interpreted with caution. Additionally, EEG has a limited spatial resolution compared to over-neuroimaging techniques, and further investigations with fMRI could further support the findings and explore the spatial distribution of neural activity. Similarly, advanced EEG processing, such as the application of Spiking Neural Networks (SNN) to explore differences in connectivity throughout brain data, should be considered in future research.

Furthermore, the continued advancement of analytical techniques for electroencephalography (EEG), particularly machine learning (ML) and neural network analysis, presents promising avenues for future research in understanding Functional Neurological Disorder (FND). ML techniques, such as supervised and unsupervised learning, offer opportunities to uncover hidden patterns and infer valuable insights from complex EEG data (Ghahramani, 2015; Kotsiantis et al., 2007). Supervised learning methods leverage

existing and estimated target values to develop predictive models, whereas unsupervised learning techniques cluster data based on similarities, revealing unknown patterns and structures. Additionally, spiking neural networks (SNNs) represent a novel application that extends beyond conventional ML approaches, enabling the training of data to interpret spatial and temporal information and create three-dimensional models mapping brain structures (Indiveri et al., 2015). SNNs simulate the brain's natural processes by incorporating artificial spiking neurons capable of learning from temporal data and integrating time into their computational operations (Agatonovic-Kustrin & Beresford, 2000; Schmidhuber, 2015). By applying SNNs to EEG data, researchers can model and extract new knowledge from spatiotemporal dynamics, offering a more biologically plausible approach to understanding brain function (Gholami Doborjeh et al., 2018). These advancements hold significant promise for enhancing our understanding of FND by providing deeper insights into the dynamic interactions and patterns of brain activity underlying the disorder. Whilst there was insufficient time or space to include these techniques in the current thesis, future research endeavours could leverage these techniques. These have the potential to reveal novel biomarkers, refine diagnostic criteria, and develop targeted interventions for individuals with FND, ultimately transforming the landscape of FND research and clinical practice.

8.9 Thesis conclusion

In summary, this thesis demonstrates that there are psychological, neurophysiological and neurochemical differences in FND and that these could result in distinct disorder subtypes. Specifically, dissociation, an often-overlooked concept in contemporary models, was elevated throughout the studies presented here. Dissociation should be considered as a core construct in FND, and this holds a relationship with many other psychological facets in chronic illness, some of which are more specific to FND. The presence of distinct subtypes of FND was noted through latent class analysis. Some subtypes were noted as having a relationship to predisposing factors and dissociation. Collections of symptoms can characterise each of the seven distinct subtypes, and further research should consider expanding upon this further in the hopes of capturing further subtypes and being reflective of patients' lived experiences.

The thesis also demonstrates the role of inflammation in FND and its relationship to dissociation. Inflammation is elevated in those with FND, and further work could establish the

distinct neurochemical profile of FND and implicated inflammatory pathways. Some of these inflammatory markers were influenced by dissociation and mood and other elements more typically associated with general chronic illness (such as life changes, reduced activity, etc). However, this did not influence IL-6, and as such, there could be at least two implicated inflammatory pathways which warrant further investigation.

Brain activity baseline differences were found in FND. This has implications for the usefulness of EEG in investigating FND and adds to the growing body of knowledge in this area. Particular frequencies denoted higher and lower connectivity, suggesting specific neural dysfunction and signatures in FND that need further investigation. These, too, in some cases, held a relationship to dissociation and inflammation.

Taken together, the thesis suggests that an embodied brain model is a novel way of conceptualising FND. This acknowledges the bidirectional interactions involved in the neuropsychological, neurobiological, neural network, and neurophysiological processes involved in FND. This thesis highlights essential insights into this relationship and how these can further inform the dynamics and unique neurobiological mechanisms of FND. This work offers an improved understanding of the neurophysiology of FND and the necessity for the application of multimodal studies to develop this knowledge.

Chapter 9: Reflections on Belonging: Academia, Identity, and the Patient-Researcher Experience

9.1 Chapter Introduction

Academia prides itself on the pursuit of knowledge, objectivity, rationality, and the idea that research exists in a vacuum, untainted by the biases, struggles, and lived experiences of those who conduct it. But the reality is far messier. No research is ever genuinely objective because researchers are not blank slates. We bring ourselves, our identities, our histories, and our challenges into our work, whether we acknowledge it or not.

When my examiners suggested a reflection on my PhD journey to be included in my thesis, they framed this around the impact of the pandemic. The disruptions to research, the shift to remote work, the need for resilience in uncertain times and the project plans that shifted along the way. However, to limit this reflection to the pandemic alone would only be part of the story for me. Because the truth is, I was navigating this PhD as an outsider long before COVID-19 arrived.

This chapter, therefore, is about conducting research during a global crisis (a reflection that I am sure my peers would resonate with). However, it is also about what it means to complete a PhD while being a patient myself, a mother, a woman of a working-class background in a field that often asks for detachment where I could only bring lived reality. It is about holding (and juggling) multiple identities at once:

- A patient-researcher studying a condition I experience while trying to remain 'objective' in pursuing scientific rigour.
- A single mother balancing a PhD with childcare, financial instability, and the knowledge that traditional academia was not built for people like me.
- A working-class academic and first-generation student learning the unspoken rules of a system that assumes a level of social capital I did not have.
- As an individual who was rebuilding from personal upheaval, I was carrying the weight of responsibilities far beyond research deadlines.

For me, the Ph.D. was not just an academic challenge; it was deeply personal and six years of my life. It was a test of endurance, a negotiation between the structures of academia,

the unpredictable and often chaotic nature of life, and the negotiations I had to make along the way.

Reflection is often positioned as second in research, something to be tucked away and conducted privately and rarely published for the world to read, or simply a small nod to the 'challenges encountered' before moving on to the *real* work. But autoethnography challenges this idea and positions personal experience as not a striction from research but an essential part of it (Adams et al., 2017; Butz & Besio; 2009; Ellis et al., 2011). During my PhD, I initially grappled with the tension between subjectivity and academic rigor, unsure how to navigate my dual role as both researcher and patient. It was only through engaging with autoethnography that I began to see my lived experience not as a methodological weakness but as a legitimate and valuable lens of inquiry. As Wall (2006) describes, the process of learning autoethnography itself is a deeply reflexive and sometimes unsettling journey, one that challenges conventional notions of objectivity while demanding a level of self-examination that is both intellectually and personally transformative.

To structure this reflection, I draw on several reflective models. I draw on Gibb's Reflective cycle (1988) as an homage to my students whom I encourage to use the model often, and which provides a systematic way of examining experiences through six stages: Descriptions, Feelings, Evaluation, Analysis, Conclusion, and Action. I will also integrate Schon's (1983) concepts of reflective practice, distinguishing between reflection in action (how I adapted in the moment) and Reflection in action (looking back at moments of challenge to extract deeper meaning and insights). By applying such frameworks, I move beyond my brand of personal storytelling (somewhat) into a critical exploration of how my journey shaped not just my research but my understanding of academia and my own practice itself.

PhDs are often framed as intellectual pursuits, but the reality is that they are deeply personal journeys, shaped by life within and beyond academia. This chapter is a reflection not just on the barriers I faced but on the ways in which those barriers reshaped my understanding of knowledge, the transference of knowledge, resilience and identity. It is also an argument (because it would not be me elsewise) that personal experience does not invalidate research but strengthens it; academia should recognise the realities of those who do not fit its traditional mould, and that reflection should not be an afterthought but a critical tool in knowledge production itself. This is not just a story about my PhD, but a recognition about what it means

to pursue knowledge while holding multiple, and at times conflicting, identities simultaneously. Perhaps, most importantly, it is a reflection on why systems must change.

9.2 Chapter overview

This chapter explores key moments of my PhD journey, structured around the major challenges, transformations, and insights that defined it. I have divided it into 6 key sections.

- **Navigating Academia as an outsider –** Learning the unspoken rules of a world that I never believed I belonged in.
- **The Patient-Researcher Paradox** – The tension between studying a condition I experience while maintaining academic 'objectivity'**.**
- **Single Parenthood and the PhD** – The reality of balancing academia with caregiving.
- **The Pandemic as a Disruptor and Catalyst** – How the COVID-19 pandemic both complicated and clarified my journey.
- **Finding my Voice –** overcoming imposter syndrome, embracing advocacy and learning that I did not need to erase parts of myself to succeed.
- **Recommendations –** drawing meaningful conclusions based on this reflection.

9.3 Reflection Introduction

Early in my PhD, my son was small enough to sit on my lap whilst I worked. I remember precise moments of one adorably chubby hand gripping his bottle, the other lovingly tangled in my hair, sticky with whatever remnants of the day clung to his fingers. I would read my drafts or papers aloud, trying to balance my roles, my voice reading scientific notes in a voice soft enough to soothe him to sleep but clear enough that I could still hear the shape of my own arguments or those on the page. Somewhere at the back of my mind, I'm still trying to think of the plans I have for the evening; my productive time can begin the moment I settle him to bed. It was an imperfect system, but it was mine and the only way in which I could operate. Now, seven years on, he leans against me in a different way – longer limbs, heavier presence, his arm draped casually over my shoulder as he loses himself in the small, pixelated world of his Nintendo DS. I work as he rests, still weaving my words around the weight of his presence

(though now he can read, he occasionally reads aloud a sentence he feels I have mistyped or one that he has an opinion on). Yet here I am, still balancing the dual roles of researcher and mother. The landscape now, however, has shifted. This reflection is about that shift, not just the passage of time, but the evolution of identity, the way a PhD is never just about research, but about the person you become while writing it.

When my examiners suggested a reflection, it was framed around the pandemic – its disruptions, its forced adaptions, the ways in which we learned to work in isolation, to recalibrate our expectations of progress. And while that is certainly part of this story, it is not the whole story. Because resilience did not begin with the pandemic, and it did not end with it. This reflection extends beyond the logistical challenges of remote research. It is about navigating academia as an outsider, about learning the unspoken rules of a world that was never built with people like me in mind. It is about the tensions of dual identity, being both a patient and a researcher, both a single mother and an academic, both the one producing knowledge and the one scrutinised by it. At its heart, this is a reflection on what it means to belong in spaces that were not designed for you and the ways in which we carve out space anyway.

Throughout this piece, I explore:

- The pandemic as both disruption and revelation - The forced isolation of lockdown made the invisible visible, bringing into sharp focus structural inequalities that existed long before the pandemic.
- The resilience of patient research - the duality of researching a condition while embodying its lived reality and the tensions this creates in an academic world that historically privileges detachment.
- The shifting identity of the academic parent – balancing a PhD with single parenthood, moving from a lap-held toddler to a growing child who has, in his own way, grown up alongside my research.
- The importance of advocacy and inclusion – why representation in academia matters and how those of us who enter these spaces from the margins must often build the bridges we need.

While this is deeply personal, my reflection extends beyond this. Autoethnography teaches us that experience is not merely anecdote but data and that lived experience offers insights that cannot be accessed through distance alone (Wall, 2006). To structure this

reflection, I draw on Gibbs' Reflective Cycle (1988) and Schön's (1983) model of reflective practice, both of which allow for a systematic exploration of experience. This is not just what happened but what it means, how it shaped me, and how it informs my work moving forward. More than anything, this is a reflection on endurance, on persistence, on what it means to sit in the uncomfortable spaces and remain anyway. Academia, traditionally, may not have been built for people like me. But here I am. And I am staying (with my own brand of Chaos).

9.4 Navigating Academia as an outsider

When I entered academia, I felt like a trespasser, tiptoeing into a world that wasn't built "for people like me" and feeling like I did not belong. The first in my family to go to university, I knew that knowledge (or at least the access to it) was a privilege, one that I could only access if I learned how to move invisibly, quietly, correctly. At first, I tried to decode the language of academia through observation, absorbing every unspoken rule like an anthropologist would in an unfamiliar culture (Bourdieu, 1984). Nevertheless, no matter how well I studied the customs, I always felt like I was mimicking, never genuinely belonging in a place that I truly longed to belong in.

There is a moment, rather trivial in hindsight, that sticks with me still: a conversation about halloumi cheese in the shared kitchen. I already felt like an imposter, straight out of my undergraduate studies, but I landed a role as a research assistant on a huge multi-study project that had landed so much funding and I, so much responsibility. But there, in the kitchen, the group was animated, debating the squeak factor, discussing the best brands, and comparing halloumi to other cheeses. I stood there, silent. Not because I had nothing to say but because I had no reference point, no shared history of dinner table debates about "premium cheeses," and I felt like I was missing some kind of internal joke that the rest of the group knew of. It was not about cheese. It was about cultural shorthand (Bennet, 2017) and an invisible test of belonging that I had already failed. This moment, though minor, reflects Bourdieu's (1986) concept of cultural capital, where knowledge, language, and social cues act as forms of power. Academia assumes a certain baseline familiarity with these codes, ones that working-class students often find themselves learning on the spot rather than inheriting.

The discomfort wasn't just social; it was existential. Whenever I spoke in a seminar or at a research group later in my career, I felt the weight of proving I deserved to be there. If I spoke

too assertively, I was “too aggressive” or “too egotistical”. If I softened my stance, I was “uncertain”. If I admitted I struggled, I would be proving the doubts I already feared others had of me. Academia is a world where confidence masquerades as competence (Moutntz et al., 2015), where the correct vocabulary, the right tone, and the right knowing smirk in a discussion can establish your credibility. However, I did not know the rules of the game, let alone how to play it convincingly. Prior to my PhD, I had already spent years balancing being a single mother, a patient, and a researcher, but those identities were not visible when I walked into a room. Instead, I was measured against standards built for those who never had to fight just to sit at the table in the first place.

At times, through my journey, I have felt as though I was dismantling myself into socially acceptable pieces, cutting away the raw edges of my experience to fit into a mould that was not designed for me. Research has shown that working-class students and academics often engage in this ‘code-switching’ to assimilate into academic culture at significant psychological cost (Reay, 2018). I changed the way I dressed, the way I spoke. I had to be corrected on formalities in email tone or voice projection, all the while people did not see that it was because I had not been taught these acts. I learned to self-edit in real time, constantly scanning for cues about how much of myself was safe to reveal. Ahemend (2012) describes the constant “sweating” of those who do not fit, an awareness of being hyper-visible while simultaneously invisible in decision-making spaces. Nevertheless, still, despite my efforts, I was still seen as an outsider.

The irony is that I entered this field precisely because of my personal connection to my research. My work was not just academic; it was deeply, intrinsically personal. I studied Functional Neurological Disorder (FND), inflammation and dissociation, not just because they were intellectually interesting, but because they were a part of my body and my reality. However, objectivity is a currency in academia, and personal experience is often seen as an intellectual liability rather than an asset (Harding, 1991). My lived and felt knowledge was dismissed in favour of detached observation. When I pointed out patterns in patient narratives were not always accounted for in the literature, I was met with scepticism in some places, even condescension. At a time in a research seminar, someone dismissed a patient’s subjective account as “anecdotal”. I sat there, feeling the weight of my own experience in my throat, knowing that in their eyes, I was an anecdote too. This is a well-documented issue in research, epistemic injustice, where lived experience is seen as secondary to ‘expert’ knowledge (Fricket, 2007). Patient narratives are often framed as interesting but unreliable, even though those with firsthand experience often hold the deepest insights into their own conditions (Greenhalgh,

2016). It was here, in this paradox, between being a researcher and being the subject of research, that I found the deepest tension in my academic journey.

It was not an institution that gave me permission to belong – it was people. One of them was Prof. Eva Sundin. She took it upon herself to become my informal mentor and saw in me what I had not yet learned to see in myself. She never asked me to shrink or to filter my experiences to fit academia's standards. Instead, she helped me to understand that the things that made me feel like an outsider were also my greatest strengths. Mentorship is crucial for students from underrepresented backgrounds. McAlpine and Amundsen (2011) highlight the importance of academic mentorship in building confidence, particularly for those navigating imposter syndrome. Having someone validate your perspective, not despite your background but because of it, can be transformative. Eva passed away before I finished my PhD. She never saw the end of this journey. Nevertheless, her presence is embedded in every word I write.

I was also fortunate to have a supervisory team that recognised my potential and supported my progression. My director of studies, Prof. Alex Sumich, has guided me from my undergraduate degree, then to my master's and finally onto my PhD. Alex once told me that he stood on the shoulders of giants, and now, in the role of a senior lecturer, I can appreciate his sentiment. Alongside him, Christina Howard and Suvo Mitra played an invaluable role in my PhD. Their support of my academic progression was matched by their concern for my well-being. They provided me space to navigate this journey and its complexity as a team. I feel that in some way, by recognising the unique aspects of my journey and some mirroring their own experiences, they were able to provide me space and the ability to recognise my potential beyond my academic output. It was never just about the research – it was also about the person behind the research.

I no longer write or speak with the intention of proving that I belong here. I belong here because I am here. I have stopped dismantling myself into palatable pieces. Instead, I bring all of it – the patient, the researcher, the single mother, the advocate. I no longer try to contort myself into a version of professionalism that demands detachment. Instead, I claim the space never designed for me and reshape it in my own image. Traditionally, academia asks us to strip our work of emotion, of self, as if knowledge can only be formed in sterile, detached spaces. However, Harding (1991) argues that all knowledge is situated; objectivity is not achieved through detachment but through acknowledging one's positionality.

Now, as a Senior Lecturer, my lived experience informs not just my research but also my pedagogical approach. My teaching is shaped by critical pedagogy (Freire, 1970), the idea that education should be a practice of liberation rather than assimilation, challenging traditional power structures rather than reinforcing them. I do not just teach my students to absorb knowledge; I encourage them to question the producers of knowledge, whose voices are included and whose perspectives are silenced. Like Bell Hooks (1994), I believe that education should be transformative and that the classroom should be a place where lived experience and academic knowledge are in dialogue, not opposition. This is particularly critical for students from underrepresented backgrounds, who, like I once did, may feel that their struggles make them less suited for academia. I try to encourage the realisation that their experiences offer perspectives that academia (and clinical practice) desperately needs. I integrate inclusive pedagogical practices into my teaching, encouraging students to reflect on how their positionality shapes their academic work (Cook-Sather, 2014). I draw on asset-based approaches that reframe challenges not as deficits but as sources of insight (Yosso, 2005). My goal is for students to leave my classroom not just with knowledge but with the confidence that they, too, have a place in academic and professional spaces.

Academia should not be about erasing personal struggles but learning from them and using them as a force for change. The more I teach, the more I see this in practice. The students who come to me doubting whether they belong are often the ones who bring the most profound insights. I write this not just for myself but for the next researcher/s who sit in silence in a shared kitchen, wondering if they are an imposter in a world of halloumi conversations. You belong. The world will catch up with that fact soon, too.

9.5 The Patient-Researcher Paradox

I have read descriptions of my own conditions in textbooks, journal articles and clinical reports, but never in my own words until undertaking research. At one point, I became paralysed by the act of writing itself, trapped in a kind of intellectual imposter syndrome. How could I feel like an outsider to a condition I had both studied and lived? How could I fear misrepresenting something that shaped my own body, my own life? And yet, I did. For most of my academic journey, I encountered my body not as a site of knowledge but as an object of study (and dysfunction and chaos). Something dissected in medial literature's cool, detached

language, framed through the lenses of dysfunction, conversion and deficit. I remember reading an early paper on FND that outlined a clinical presentation eerily similar to my own (so similar, in fact, that I remain convinced it was about me). It should have been an intellectual exercise, but instead, it felt invasive, like standing outside of myself while a room full of experts discussed my body as though I were absent. Nevertheless, I knew what that felt like, too. I had already lived that moment.

When I was first diagnosed, I lay in a hospital room, unable to move, unable to speak, trapped in a body that no longer responded to me. I heard them before I saw them; the clinicians gathered at my bedside, speaking over me, about me, as though I were not there. I heard the doubt in their voices, the causal speculation:

"*She's a teenager."*

"Maybe she just wants attention."

"If we leave her long enough, maybe she'll snap out of it."

I wanted to scream. I wanted to move, to make them see that I was not invisible, not pretending, not absent from my own body. But I was trapped. Stuck between medical scepticism and the undeniable reality of my own experience. Years later, as I sat in front of my PhD (or the blank page that would eventually become my thesis), I found myself in a similar state of paralysis. How do you write with authority about something that has, at times, rendered you voiceless? How do you position yourself as an expert in a condition that academia insists you can only study at a distance? That is the paradox of being both a patient and a researcher. The closer you are to your subject, the more you are asked to prove your legitimacy. To strip away the personal. To perform detachment. To dissect yourself.

This is the paradox of being both patient and researcher. You learn to toggle between identities. Between being the subject and investigator, between the dispassionate voice of academic writing and the deeply embodied experience of living with the very condition you are analysing. It is a paradox that is not easily resolved because academia, historically, has built the foundation of detachment as a marker of legitimacy (Haraway, 1988). The patient-researcher model challenges this deeply embedded norm, forcing a confrontation with the question: Who is allowed to produce knowledge?

From the outset of my PhD, I was aware that my lived experience would be both my greatest strength and my greatest liability. It gave me insight into patterns that traditional

research often overlooked, but it also placed me in a position where I would need to justify my place at the table, not only as a scientist but as a subject. There is an implicit hierarchy of knowledge in academia, one that privileges the detached observer over the embodied knower (Carel & Kidd, 2014; Fricker, 2007). Lived experience is often relegated to the realm of anecdote – interesting but perhaps not scientific. I felt the weight of this dynamic often, and I hesitated to speak out. Even at conferences, I wondered if mentioning my diagnosis would undermine my authority. In a seminar discussion, for example, a fellow researcher dismissed a patient narrative as "purely anecdotal". I sat there knowing that in their framework, I too was anecdotal. No matter my research's rigour, my lived experience threatened to destabilise my growing credibility. This scepticism toward patient-researchers is part of a broader issue of epistemic injustice in medicine, the systematic devaluation of patient knowledge in favour of institutional authority (Carel & Kidd, 2014). Patients often feel unheard in clinical settings, their accounts are scrutinised more than their diagnostic tests, and their words carry less weight than their medical records. In academia, as in medicine, the patient is expected to be the passive recipient of knowledge, not its producer.

However, what if that framework is wrong? What if the lived experience of illness does not taint research but enriches it? What if the knowledge held in bodies, narratives, and communities of patients advocating for themselves is just as valid, if not more so, than the knowledge in textbooks? Feminist epistemologists have long argued that all knowledge is situated and that objectivity is not the absence of bias but the awareness of one's positionality (Harding, 1991; Haraway, 1988). I began to realise that my role was not to suppress my experience but to integrate it critically, to interrogate where lived experience intersects with empirical data and where it challenges those dominant narratives. I would love to say that there was a critical moment where this realisation occurred, but there was not; it happened slowly and with time. As my PhD progressed, so did my confidence in this perspective. I began to see what others had missed, like patterns in patient narratives that aligned with neurobiological findings or could be experimentally explored and inconsistencies in theoretical frameworks that could only be noticed when lived experience was considered. I was no longer simply collecting data; I was interpreting it through a lens that traditional researchers did not have access to. The shift was gradual, shaped by conversations with others, by my increasing involvement in advocacy, and by moments where I saw firsthand the gaps in academic knowledge that would only be filled by those who had lived it.

The expectation that knowledge should be gathered, observed, and analysed from a safe intellectual distance was not one that would fit my direction. Despite this, personal experience (particularly in medical and psychological sciences) remains commonly seen as a contaminant rather than an asset (Haraway, 1988). This is the Cartesian legacy of mind-body dualism, where scientific legitimacy is tethered to detachment and objectivity, as though the body is an unreliable narrator of its own experience (Wendell, 1996). Yet this creates a fundamental paradox for the patient-researcher and for the progression and advancement of many fields. Continued practices create epistemic injustice and marginalise embodied knowers who should be central to knowledge production rather than discredited. This tension in my own research manifested in tangible ways. Though I hesitated initially, I could move through critical self-reflection and change how I performed research. Though I recognised the paradox and the constant negation between the boundaries of scientific analysis and personal insight, I felt conflicted. I began to recognise that the tension between embodied knowledge and academic authority was not a failure of my research or myself but a failure of the system that defines expertise. The rejection of lived experience in the medical sciences reflects broader historical trends, where patient voices have been excluded from shaping medical discourse (Greenhalgn, 2016). I began to see my perspective not as a bias but as a methodological strength, aligning with contemporary movements in narrative medicine and patient-centred research (Charmaz, 1991). I no longer sought to distance myself from my research but instead acknowledged it as situated knowledge and integrated my perspective more critically (Haraway, 1988).

While the traditional academic model has historically excluded patient voices, there is a growing movement toward participatory and co-produced research that actively integrates lived experience into study design, analysis, and dissemination (Greenhalgh et al., 2019; Madden & Speed, 2017). Participatory Action Research (PAR) and co-produced methodologies challenge the traditional researcher-subject hierarchy, recognising that those with a lived condition hold expertise that is complementary to clinical and academic knowledge (Cargo & Mercer, 2008). This shift is particularly evident in patient-led research initiatives, which value experiential knowledge as integral rather than supplementary to scientific inquiry. This also aligns with broader changes in medical humanities and narrative medicine, which are that stories are not just personal reflections but legitimate sources of data (Frank, 2013). Rather than reducing patient experience to “anecdote”, qualitative research and phenomenological approaches increasingly highlight the necessity of integrating first-person accounts into medical and psychological science (Mattingly, 2010). My own research was situated at the

intersection of these tensions. While I had entered academia expecting to distance myself from my condition, I ultimately realised that patient-researchers hold unique epistemic authority – not because of bias, but because our lived experience allows us to see things that conventional researchers might miss. However, whilst these shifts toward participatory methodologies are promises, they are not yet fully embedded into the academic mainstream. The tension remains: whose knowledge is considered legitimate, and whose is still considered secondary?

My shifting thoughts on this topic did not happen in isolation but were ultimately shaped by direct involvement in patient advocacy, the third sector, and interdisciplinary conversations in medical humanities. Schön's (1983) concept of 'reflection-in-action' captures this transition well. Through advocacy work, I was no longer just reflecting on my role in academia but actively reshaping it in real time. This became clear when I stepped onto a TEDx stage, delivering a talk that did not just outline my research but positioned patient narratives as central to medical knowledge production. In my role as Vice-Chair at FND Dimensions, I was no longer negotiating my position as an outsider. Instead, I was contributing to systemic change, challenging structures that had once made me question my legitimacy in academia and opening the doors for others who wanted to access higher education. I have also begun to produce systems whereby patients' experiences are heard and listened to and wherein they become the producers of knowledge that ultimately support others in the community. These moments did not erase the patient-researcher paradox, but they reframed it. No longer was it a limitation to be managed but an asset to be fully claimed. This is, for me, the direction academia must move toward – one where expertise is not defined by detachment but by the integration of critical lived perspectives into research.

9.6 Single-Parenthood and the PhD

My son has never known a life without my PhD. When I started, he was barely two and small enough to fit against my chest as I typed, his breathing slow and steady while I proofread journal articles one-handed. Now he is eight, long-limbed and independent (well, mostly), stretching into the world while I try to balance academia with the responsibilities of raising him alone. Single parenthood was never an incidental factor in my PhD; it shaped every aspect of my experience, not just in time and resources but in identity. The duality of roles as a researcher and a mother, academic and caregiver, was a constant negotiation, a shifting of

priorities that my PhD did not wait for and that others failed to recognise as legitimate. In a seminar once, a peer suggested adjusting my priorities and being at home with my child. Others have critiqued my inability to prioritise when my little one falls unexpectedly ill or when I attend a professional event with an unexpected food smear across my shirt. The chaos of the role was never the thing that bothered me the most, but the perceptions of others (or that others felt that they could have) when I became a mother and continued to pursue my career did. Who knew that informing someone you could not do something because you were a single parent would lead them to ask "Why?" or question your legitimacy or have an opinion on what you should be doing when they themselves have never experienced this? Or expect you to inform them of the traumas openly that have led to you raising a child alone?

Though the chaos certainly did exist. While some of my colleagues spoke of 'immersing' themselves in their research, losing entire weekends to deep intellectual thought, I did not have that luxury. My days were not marked by the ebb and flow of research productivity alone but by school runs, meal planning, bedtime routines, and the ever-present hum of financial responsibility. In this, my experience aligns with Sime and Sheridan's (2014) research on the academic parent paradox, where the expectations of productivity in academia conflicted with the non-negotiable realities of caregiving. Motherhood is rarely factored into the structures of higher education, and even less so is single parenthood, where every responsibility is concentrated in one person. I always negotiated time, space, and energy, constantly to-ing and fro-ing between competing demands.

Beyond time, there was the inevitable financial strain. Unlike many of my colleagues who could rely on additional income from partners or family support, I bore the full weight of financial responsibility. Academia is not designed for financial precarity. PhD funding is often modest, contracts for academic work temporary, and childcare remains an exorbitant cost that is rarely accounted for in institutional policies (Moreau & Bernard, 2018). To sustain both my research and my child, I worked alongside my PhD, taking additional academic roles, picking up research assistantships, and later moving into lecturing before my thesis was even complete. The concept of an "ideal PhD candidate" assumes financial stability and the ability to work full time on research without the interruptions of employment or caregiving. However, as Lynch (2010) notes, this assumption is built upon middle-class privilege and male-dominated academic norms, where the invisible labour of parenting is either outsourced or not a problem.

The invisibility of care work in academia is a key site of feminist critique. As Guenther et al. (2021) highlight, single mothers in academia face a double bind: They are expected to be both fully committed to their research and fully available to their children. The lack of structural support means that they often compensate through overwork, stretching themselves across academic and domestic labour in mentally, emotionally, and physically unsustainable ways. I certainly remember staying up late for hours on end to complete tasks when my little one slept and juggling competing demands. It also has implications for career progression. Though expected to present at conferences and travel, such things are not possible for those in a single-parent position. Often, financial support is not provided or is limited to transport costs. For me, the financial strain was not just about income but also about the mental burden of ensuring we had enough. There was no room for failure, no option to pause my studies for financial reasons without serious consequences for both my career and my child's stability. And yet, despite this, financial hardship is often framed as personal failing rather than continued structural issues.

Academia has long operated under the illusion of the "ideal researcher", the detached, fully committed scholar who exists solely to pursue knowledge (Grant et al., 2004). This ideal assumes total availability to the institution, a capacity for evening seminars, weekend or even midweek conferences, and the kind of all-consuming intellectual work that is incompatible with caregiving (statistical analysis and re-runs of Shuan the Sheep on Netflix are, in my opinion, two things that should never have to go together). In contrast, single parents in academia operate within constant constraints wherein time is fragmented, availability is negotiated, and research is fitted into the spaces left behind after all other responsibilities. Shaw and Ward (2014) describe this as the "motherhood penalty" in academia, where parents face reduced opportunities for career advancement due to caregiving constraints. It is no wonder I felt lost in this process, and could not formulate the separate parts of myself into a coherent narrative structured around a clear sense of self, belonging and identity. Much of life has been "on hold" as a result and I feel the weight of this still even whilst finalising my submission.

This was particularly evident during the pandemic. While some researchers found themselves with unexpected writing retreats during lockdown, I was balancing full-time childcare, homeschooling and research (and had taken a temporary role with the Covid-19 foresight committee) without a support system. Though I remain grateful to some of my peers who had equally poor sleep patterns and who would meet me online, late at night, to perform virtual writing retreats. Research by Minello et al., (2021) found that during the pandemic, academic mothers reported a sharp decline in research productivity, widening an already

significant gender gap in higher education. There is a cognitive dissonance in academia's approach to single parents. Universities celebrate stories of perseverance and resilience yet often provide little structural support and often no policies that acknowledge the reality of single-parent PhD students (e.g. funding adjustments, childcare provisions, formal recognition of the additional barriers).

I adapted, thanks to the people and support structure that I had, and I am certainly grateful that my institution did make some adaptions. This is not true for many, where barriers are invisible to the institutions but deeply tangible for those in the midst of them. I worked in bursts, early mornings before school drop-offs and late nights after my son had fallen asleep. I attended academic conferences online wherever possible with a baby monitor next to my laptop, my mind switching between research discourse and the practicalities of whether my child was settling for a nap. Through Schon's (1983) model of reflective practice, I came to recognise that my approach to academia – working in fragmented, adapted, and non-linear ways- was not a failure but a different way of existing in research. My experience was not one of deficiency but of innovation, finding a way to navigate. Going forward, I refuse to measure success against a model that was never built for me. Success is not measured by proximity to an outdated ideal but by the ability to redefine academia in more inclusive, representative ways. I certainly hope I have begun doing this for my students and those going through their undergraduate or master's thesis work who have caregiving responsibilities. Beyond this, I recognise that the PhD was never just mine. It was ours, mine and my son's. In that, I have already succeeded.

9. 7 The Pandemic as a Disrupter and a Catalyst

I remember, half-jokingly, telling a colleague, *"I could do with two weeks at home."* When the threat of the potential first lockdown was upon us, it was a passing remark, one of those offhanded wishes for a pause, just long enough to catch my breath, to slow the relentless pace of research, work and parenting. I had no idea that the entire world was about to stop. When the pandemic arrived, it did not simply delay my research. It upended it. The day before the lockdown was announced, my EEG experiments (three task-based paradigms) had successfully (finally, after nearly a year of coding) run in their first pilot, and my phlebotomy equipment was all set up and ready to go. Suddenly, I was not just a PhD candidate navigating

methodological complexities; I was a researcher in a world that was actively rewriting its own rulebook in real time. The longer the lockdowns went on, the more my designs had to change. Ethics procedures shifted, participant recruitment became impossible, and the data collection painstakingly planned over months was indefinitely postponed. Yet, in that disruption, something unexpected happened. The pandemic did not just obstruct my PhD; it transformed it.

Though the pandemic obstructed my research, it also created opportunities which have profoundly shaped my academic and professional trajectory. During this period, unable to do my research, I worked with the COVID-19 Foresight Team. Not only did it promise to provide me with a short extension, funded, to my PhD and give me some financial security, but I also had the opportunity to contribute to policy development, crisis response strategies, and public health research and planning. The skills I had honed during my PhD, like critical analysis, health research, and psychological insight, became directly applicable to a global crisis. This experience placed me at the intersection of health policy and research application, providing an entirely new dimension to my academic identity. Theorising about health disparities in research is one thing, witnessing the direct impact of health crises on real populations is another. The work I did with this team deepened my understanding of the social determinants of health, crisis response and the systemic vulnerabilities within public health infrastructures (Bambra et al., 2020). More than that, it reshaped my understanding of my own research, reinforcing that real-world application must sit alongside academic inquiry. The pandemic restructured my understanding of research, crisis and resilience, but it would take much longer for me to apply those lessons to myself.

By the time the world began to return to normal, I had finished my work with the foresight team, resumed my PhD and teaching at full capacity, and re-entered academic life at full speed. While many had taken the pandemic as an opportunity to slow down, to rest, to recalibrate, I had done the opposite. I did not take the time to pause because it did not feel like an option. I had adapted, pivoted, and moved forward, driven by the urgency of both my research and my responsibilities. I will admit that the pandemic and the fears it brought were difficult to process, too. I was driven by anxieties about my health, that of my son, the risk of infection (and was alerted to being part of the "extremely vulnerable population", a label which I did not want as I was reminded that I was ill and recovering from surgeries still). This anxiety drove and fed my already-burning imposter syndrome, and I drove it into research as a means of coping. It was only later, when my health shifted further in ways I could no longer ignore, that I

recognised what I had missed. A new diagnosis, one that I chose not to focus on here, but which fundamentally reshaped my perspective, forced me to confront something that I had long resisted: the need to slow down, intellectually and physically.

It was ironic in some ways. The pandemic has taught the world to pause, but I only learned the lesson after the world had moved on. Lupton (2020) describes the pandemic as a rupture in the way people relate to their own bodies – a moment that forced many to re-evaluate their relationship with health, time and personal limits. For me, that rupture came not during the pandemic but after it. I felt guilt when I realised how much I had pushed through, and the experience of illness became a personal embodiment of what I had studied in health research – the disconnect between knowledge and lived behaviour. Broadly, the culture of academia and the crisis response do not often reward rest but endurance, and I had internalised this (likely a result of my previously mentioned feelings of imposter syndrome). Only later did I see the consequences and lesson the pandemic should have taught me: Rest is not an indulgence but a necessity. I am now more intentional about balancing research, advocacy, teaching and health, recognising that contribution is not just about productivity but also about sustainability.

I began my PhD believing in certainty, research plans, structured methodologies, and tightly controlled schedules and environments. The pandemic dismantled that illusion, revealing a world where research must be responsive, adaptable, and engaged with real-world complexity. It was not only my research that had to adapt, but I also had to adapt. Disruptions from the pandemic taught me resilience, flexibility and the urgency of real-world application. My new diagnosis forced me to consider things more deeply, the way I valued my health within that system. Rather than seeing this period as a setback (which undoubtedly set me back a few years), I now recognise this as one of the most defining aspects of my PhD journey. It forced me to confront long-held assumptions about research certainty, methodological control, the false distinction between theory and practice and my identity as an academic. It forced me to confront my own assumptions about what it means to endure, contribute, and rest.

9.8 Finding My Voice

A peculiar silence comes from building your career in academia – hesitation, waiting until you feel you have earned the right to speak. For much of my PhD, I carried that silence. I was a researcher studying a condition I lived with: a single mother competing with demands, a

first-generation academic with a working-class background in a space filled with unspoken rules. I wrote carefully, too carefully, each sentence measured, each argument hedged, afraid that too much certainty would expose my blind spots, but too much caution would betray a lack of confidence. Every email I had to write induced in me the kind of anxiety one would expect if being chased by a bear in the woods. I saw in myself, and continue to see in many early-career researchers, the paradox that authority in academia must be earned through years of meticulous study rather than the legitimacy of one's insights. This tension is well-documented in the literature on academic identity formation. Colyar (2009) describes how doctoral students undergo a process of "textual self-construction", learning how to position themselves within academic discourse while negotiating what parts of their own perspectives feel "permissible" in scholarly writing. Kamler and Thomson (2006) similarly highlight the way doctoral writing functions as a site of identity negotiation, where students must balance their developing voice against the weight of disciplinary expectations. But when do you stop waiting for permission? At what point does knowledge stop feeling borrowed and start feeling like something you own?

For me, the answer came in pieces, through moments where I spoke before I felt ready, where I stepped into spaces I was not sure I belonged, where I wrote, presented and advocated not because I felt certain, but because I finally understood that certainty was never the goal. I remember a moment when writing the early chapters of my thesis, tabs open, scrolling for the correct information. I was reading a paper and loved the author's writing style. It felt "sassy", like they were sure of their opinions and were not afraid to contradict prominent authors in the field. Wanting to mimic some of the authors' wit, tenacity, and passion (which is uncommon in peer-reviewed work), I scrolled to the top of the page to check out their bio, only to discover that the author was me. That paper came because of teamwork and collaboration, of wanting to have a voice and because writing should never be perfect – but words on a page, having a voice, and sharing insights matter.

There are other moments in an academic journey that feel like turning points, not because they change your knowledge but because they change how you see yourself in relation to it. For me, one of those moments was standing on a TEDx stage, speaking about my research and my lived experience to an audience that was not constrained by academic gatekeeping or journal peer review. The process of preparing the talk forced me to ask what mattered and what message I wanted to give. The experience was transformative; not only was this the first TEDx talk on FND, but the curators forced me to craft my speech beyond academic literature. I had spent years learning to write in the careful, detached language of academia, but on that stage, I

had to speak in a way that resonated, that mattered, that connected, and that told my story to the world while giving others in the FND community a voice. The shift was not just in how I communicated but in how I conceptualised my role as a researcher. Academic knowledge is often confined within institutional walls, yet the real impact happens when knowledge escapes those walls, reaching patients, policymakers and communities. This aligns with the principles of engaged scholarship (Boyer, 1996), which argue that research must not only contribute to academic discourse but also to public understanding and social change.

Imposter syndrome is a term so frequently used in academia that it has almost lost its meaning. But that sense of "imposterhood" is not just internal; it continues to be reinforced. Research on first-generation academics, women in STEM and minority scholars suggests that feelings of imposterism are not just about individual self-doubt but about the historical exclusion of certain voices from academia (Clance & Imes, 1978; Gardner & Holley, 2011). For much of my PhD, I internalised the expectation of proving my right to be here, to justify my lived experiences, methodological choices, and my very presence in academia. But slowly, I began to realise that the standard I was measuring myself against was built for a different kind of academic, a different kind of scholar. The problem was not that I did not belong, but that academia was still learning how to accommodate voices like mine. This thought mirrors the arguments made by Ahmed (2012) in "On Being Included", where she describes the way marginalised scholars are often positioned as "guests" in academic spaces, expected to conform to existing norms rather than reshape them. The reality is that academia does not need more silent participants – it needs researchers willing to bring a bit of chaos – researchers willing to disrupt, challenge and expand the boundaries of knowledge production.

Writing is not just an academic exercise; it is an act of self-authorisation. The academic system encourages emerging researchers to write in ways that are neutral, detached, and distanced from personal stakes. But as Richardson (2000) argues, all writing is situated, and knowledge is produced from somewhere, by someone. To pretend otherwise is not a display of objectivity but a failure to acknowledge the social construction of knowledge itself. This is particularly relevant in research that intersects with patient experience, disability and advocacy. Charmaz (2004) argues that traditional research paradigms often fail to capture the lived realities of chronic illness, prioritising clinical objectivity over experiential truth. Writing from a place of lived experience, then, is not just a methodological choice; it is an intervention in how knowledge is structured and who is allowed to produce it. It is with this realisation that my writing has changed. I stopped filtering out what made my perspective unique. I stopped

waiting for the elusive feeling of "enoughness" (enough expertise, enough legitimacy, enough permission). Instead, I wrote.

9.9 Reflection Conclusion

This reflection has traversed the complexities of navigating academia as a patient-researcher, a single parent, and a scholar whose lived experience both enriched and complicated the research process. It has uncovered the tensions between objectivity and subjectivity, inclusion and exclusion, tradition and transformation – tensions that are not unique to my journey but which are embedded in many others' journeys too. The pandemic, too, functioned as both a disruptor and a catalyst, forcing a reconsideration of what is essential in research, not just in terms of methodological flexibility but in the way we define expertise, recognise barriers, and support the reality of diverse scholars. This journey for me has not been about simply completing a PhD; it has been about questioning who academia is built for and who is still asked to justify their place within it.

If academia is to evolve, it must move beyond rhetorical commitments to inclusivity and embed structural changes that recognise the realities of non-traditional scholars. The following key insights emerge from this work:

1. Patient-researchers bring an epistemic richness that must be recognised as an asset, not a liability. Academic institutions and publishing bodies must move beyond outdated notions of detachment as a hallmark of credibility (Carel & Kidd, 2014). Lived experience enhances research, particularly in fields that intersect with health and patient advocacy.
2. Single parents and caregivers remain structurally disadvantaged in academia. The "ideal researcher" model assumes unlimited time and availability, creating invisible barriers to participation (Moreau & Bernard, 2018). Universities must acknowledge these realities through flexible PhD pathways, institutional childcare support and hybrid conference options.
3. PhD programmes must be designed with adaptability in mind. The pandemic exposed the fragility of rigid, linear academic timelines. Research must be crisis-responsive, allowing for alternative competition pathways that do not penalise disruptions to health or caregiving responsibilities (Greenhalgn et al., 2020).

4. Participatory and co-produced research models must become the standard, not the exception. Traditional research structures often exclude the very communities they seek to understand (Cargo & Mercer, 2008). Patient-led and participatory methodologies should be actively funded, incentivised, and valued as legitimate contributions to knowledge production.
5. Academia must embrace voice and reflectivity rather than treat them as indulgences. Knowledge is never neutral. Scholarship that acknowledges positionality is not weaker; it is more honest, transparent, and impactful (Haraway, 1988). PhD candidates and early career researchers must be encouraged to write with presence and clarity rather than suppressing their insights to fit outdated notions of authority.

This PhD began as a search for answers but ended with more profound questions, not just about the subject of my research (though I have many unanswered questions and much more research to conduct) but also about the structures that shape who is permitted to research at all. I no longer seek to prove that I belong here. I belong because I insist on my presence, because I have carved out a space where none was offered and because I have reshaped my academic practice, not to fit in with exclusionary norms, but to challenge them. In the end, the measure of a PhD is not simply in its contribution to knowledge but in how it transforms the scholar who undertakes it. This work has changed me, not just in what I know (rather in what I do not know), but in how I speak, how I write and how I claim space at the table.

If my journey is any indication, academia is at its strongest when it learns to listen. Listen to those who enter as outsiders, to those who bring lived experience, to those who challenge its unspoken rules, and to those who bring chaos. Transformation, in the end, is not just an individual act. It is the work of reshaping institutional practices moving forward to better reflect the world it seeks to understand.

References

Acharya, U. R., Oh, S. L., Hagiwara, Y., Tan, J. H., & Adeli, H. (2018). Deep convolutional neural network for the automated detection and diagnosis of seizure using EEG signals. *Computers in biology and medicine*, *100*, 270-278. https://doi.org/10.1016/j.compbiomed.2017.09.017

Adams, T. E., Ellis, C., & Jones, S. H. (2017). Autoethnography. *The international encyclopedia of communication research methods*, 1-11. https://doi.org/10.1002/9781118901731.iecrm0011

Agatonovic-Kustrin, S., & Beresford, R. (2000). Basic concepts of artificial neural network (ANN) modeling and its application in pharmaceutical research. *Journal of pharmaceutical and biomedical analysis*, *22*(5), 717-727. https://doi.org/10.1016/S0731-7085(99)00272-1

Akbey, Z. Y., Yildiz, M., & Gündüz, N. (2019). Is There Any Association Between Childhood Traumatic Experiences, Dissociation and Psychotic Symptoms in Schziophrenic Patients?. *Psychiatry investigation*, *16*(5), 346. https://doi.org/10.30773/pi.2019.02.10.2

Akyüz, F., Gökalp, P. G., Erdiman, S., Oflaz, S., & Karşidağ, Ç. (2017). Conversion disorder comorbidity and childhood trauma. *Archives of Neuropsychiatry*, *54*(1), 15. https://doi.org/10.5152/npa.2017.19184

Alayarian, A. (2019). Trauma, resilience and healthy and unhealthy forms of dissociation. *Journal of Analytical Psychology*, *64*(4), 587-606. https://doi.org/10.1111/1468-5922.12522

Ali, A. M., Alkhamees, A. A., Hori, H., Kim, Y., & Kunugi, H. (2021). The Depression Anxiety Stress Scale 21: Development and Validation of the Depression Anxiety Stress Scale 8-Item in Psychiatric Patients and the General Public for Easier Mental Health Measurement in a Post COVID-19 World. *International journal of environmental research and public health*, *18*(19), 10142. https://doi.org/10.3390/ijerph181910142

Alper, K. R., John, E. R., Brodie, J., Günther, W., Daruwala, R., & Prichep, L. S. (2006). Correlation of PET and qEEG in normal subjects. *Psychiatry Research: Neuroimaging*, *146*(3), 271-282. https://doi.org/10.1016/j.pscychresns.2005.06.008

Althubaiti, A. (2016). Information bias in health research: definition, pitfalls, and adjustment methods. *Journal of Multidisciplinary Healthcare*, *9*, 211–217. https://doi.org/10.2147/JMDH.S104807

Allendorfer, J. B., Nenert, R., Hernando, K. A., DeWolfe, J. L., Pati, S., Thomas, A. E., ... & Szaflarski, J. P. (2019). FMRI response to acute psychological stress differentiates patients with psychogenic non-epileptic seizures from healthy controls–A biochemical and neuroimaging biomarker study. *NeuroImage: Clinical*, *24*, 101967. https://doi.org/10.1016/j.nicl.2019.101967

Alluri, P. R., Solit, J., Leveroni, C. L., Goldberg, K., Vehar, J. V., Pollak, L. E., ... & Perez, D. L. (2020). Cognitive complaints in motor functional neurological (conversion) disorders: a focused review and clinical perspective. *Cognitive and Behavioral Neurology*, *33*(2), 77-89. https://doi.org/10.1097/WNN.0000000000000218

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). https://doi.org/10.1176/appi.books.9780890425596

Ani, C., Reading, R., Lynn, R., Forlee, S., & Garralda, E. (2013). Incidence and 12-month outcome of non-transient childhood conversion disorder in the UK and Ireland. *The British Journal of Psychiatry*, *202*(6), 413-418. https://doi.org/10.1192/bjp.bp.112.116707

Apazoglou, K., Adouan, W., Aubry, J. M., Dayer, A., & Aybek, S. (2018). Increased methylation of the oxytocin receptor gene in motor functional neurological disorder: a preliminary study. *Journal of Neurology, Neurosurgery & Psychiatry*, *89*(5), 552-554. https://doi.org/10.1136/jnnp-2017-316469

Apazoglou, K., Mazzola, V., Wegrzyk, J., Polara, G. F., & Aybek, S. (2017). Biological and perceived stress in motor functional neurological disorders. *Psychoneuroendocrinology*, *85*, 142-150. https://doi.org/10.1016/j.psyneuen.2017.08.023

Arbuthnott, J. (2020). *Exploring change processes in Functional Neurological Disorder* (Doctoral dissertation, University of Leeds).

Arıkan, K., Öksüz, Ö., Metin, B., Günver, G., Laçin Çetin, H., Esmeray, T., & Tarhan, N. (2021). Quantitative EEG findings in patients with psychogenic nonepileptic seizures. *Clinical EEG and neuroscience*, *52*(3), 175-180. https://doi.org/10.1177/1550059420918756

Armour, C., Karstoft, K. I., & Richardson, J. D. (2014). The co-occurrence of PTSD and dissociation: Differentiating severe PTSD from dissociative-PTSD. *Social psychiatry and psychiatric epidemiology*, *49*, 1297-1306. https://doi.org/10.1007/s00127-014-0819-y

Arnau, R. C., Meagher, M. W., Norris, M. P., & Bramson, R. (2001). Psychometric evaluation of the Beck Depression Inventory-II with primary care medical patients. *Health Psychology, 20*(2), 112–119. https://doi.org/10.1037/0278-6133.20.2.112

Arnold, B. F., & Ercumen, A. (2016). Negative control outcomes: a tool to detect bias in randomized trials. *Jama*, *316*(24), 2597-2598. https://doi.org/10.1001/jama.2016.17700

Arnsten, A. F. (2015). Stress weakens prefrontal networks: molecular insults to higher cognition. *Nature neuroscience*, *18*(10), 1376-1385. https://doi.org/10.1038/nn.4087

Asadi-Pooya, A. A. (2016). Biological underpinnings of psychogenic nonepileptic seizures: directions for future research. *Neurological Sciences*, *37*, 1033-1038. https://doi.org/10.1007/s10072-016-2540-y

Asadi-Pooya, A. A., Brigo, F., Mesraoua, B., Tarrada, A., Karakis, I., Hosny, H., ... & Hingray, C. (2020). Clinical characteristics of functional (psychogenic nonepileptic) seizures: an international retrospective study. *Epilepsy & Behavior*, *111*, 107197. https://doi.org/10.1016/j.yebeh.2020.107197

Asadi-Pooya, A. A., Farazdaghi, M., Asadi-Pooya, H., & Fazelian, K. (2023). Attention deficit hyperactivity disorder in patients with seizures: Functional seizures vs. epilepsy. *Journal of Clinical Neuroscience*, *115*, 20-23. https://doi.org/10.1016/j.jocn.2023.07.010

Ashby, F. G., Ennis, J. M., & Spiering, B. J. (2007). A neurobiological theory of automaticity in perceptual categorization. *Psychological review*, *114*(3), 632. https://doi.org/10.1037/0033-295X.114.3.632

Atienza, M., Cantero, J. L., & Dominguez-Marin, E. (2002). The time course of neural changes underlying auditory perceptual learning. *Learning & Memory*, *9*(3), 138-150. https://doi.org/10.1101/lm.46502

Atmaca, M., Aydin, A., Tezcan, E., Poyraz, A. K., & Kara, B. (2006). Volumetric investigation of brain regions in patients with conversion disorder. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *30*(4), 708-713. https://doi.org/10.1016/j.pnpbp.2006.01.011

Avbersek, A., & Sisodiya, S. (2010). Does the primary literature provide support for clinical signs used to distinguish psychogenic nonepileptic seizures from epileptic seizures?. *Journal of Neurology, Neurosurgery & Psychiatry*, *81*(7), 719-725. https://doi.org/10.1136/jnnp.2009.197996

Aybek, S., & Perez, D. L. (2022). Diagnosis and management of functional neurological disorder. *bmj*, *376*. https://doi.org/10.1136/bmj.o64

Aybek, S., & Vuilleumier, P. (2016). Imaging studies of functional neurologic disorders. *Handbook of clinical neurology*, *139*, 73-84. https://doi.org/10.1016/B978-0-12-801772-2.00007-2

Aybek, S., Nicholson, T. R., Draganski, B., Daly, E., Murphy, D. G., David, A. S., & Kanaan, R. A. (2014). Grey matter changes in motor conversion disorder. *Journal of Neurology, Neurosurgery & Psychiatry*, *85*(2), 236-238. https://doi.org/10.1136/jnnp-2012-304158

Aybek, S., Nicholson, T. R., O'Daly, O., Zelaya, F., Kanaan, R. A., & David, A. S. (2015). Emotion-motion interactions in conversion disorder: an FMRI study. *PloS one*, *10*(4), e0123273. https://doi.org/10.1371/journal.pone.0123273

Aydin, S., Dag, E., Ozkan, Y., Arslan, O., Koc, G., Bek, S., ... & Catak, Z. (2011). Time-dependent changes in the serum levels of prolactin, nesfatin-1 and ghrelin as a marker of epileptic attacks young male patients. *Peptides*, *32*(6), 1276-1280. https://doi.org/10.1016/j.peptides.2011.04.021

Ba, F., Obaid, M., Wieler, M., Camicioli, R., & Martin, W. W. (2016). Parkinson disease: the relationship between non-motor symptoms and motor phenotype. *Canadian Journal of Neurological Sciences*, *43*(2), 261-267. https://doi.org/10.1017/cjn.2015.328

Bachmann, M. C., Bellalta, S., Basoalto, R., Gomez-Valenzuela, F., Jalil, Y., Lepez, M., ... & von Bernhardi, R. (2020). The challenge by multiple environmental and biological factors induce inflammation in aging: their role in the promotion of chronic disease. *Frontiers in Immunology*, *11*, 570083. https://doi.org/10.3389/fimmu.2020.570083

Baek, K., Doñamayor, N., Morris, L. S., Strelchuk, D., Mitchell, S., Mikheenko, Y., ... & Voon, V. (2017). Impaired awareness of motor intention in functional neurological disorder: implications for voluntary and functional movement. *Psychological Medicine*, *47*(9), 1624-1636. https://doi.org/10.1017/S0033291717000071

Bailey, T. D., & Brand, B. L. (2017). Traumatic dissociation: Theory, research, and treatment. *Clinical Psychology: Science and Practice*, *24*(2), 170. https://doi.org/10.1111/cpsp.12195

Baizabal-Carvallo, J. F., Hallett, M., & Jankovic, J. (2019). Pathogenesis and pathophysiology of functional (psychogenic) movement disorders. *Neurobiology of disease*, *127*, 32-44. https://doi.org/10.1016/j.nbd.2019.02.013

Bakvis, P., Roelofs, K., Kuyk, J., Edelbroek, P. M., Swinkels, W. A., & Spinhoven, P. (2009). Trauma, stress, and preconscious threat processing in patients with psychogenic nonepileptic seizures. *Epilepsia*, *50*(5), 1001-1011. https://doi.org/10.1111/j.1528-1167.2008.01862.x

Balachandran, N., Goodman, A. M., Allendorfer, J. B., Martin, A. N., Tocco, K., Vogel, V., ... & Szaflarski, J. P. (2021). Relationship between neural responses to stress and mental health symptoms in psychogenic nonepileptic seizures after traumatic brain injury. *Epilepsia*, *62*(1), 107-119. https://doi.org/10.1111/epi.16758

Ball, H. A., McWhirter, L., Ballard, C., Bhome, R., Blackburn, D. J., Edwards, M. J., ... & Carson, A. J. (2020). Functional cognitive disorder: dementia's blind spot. *Brain*, *143*(10), 2895-2903. https://doi.org/10.1093/brain/awaa224

Bambra, C., Riordan, R., Ford, J., & Matthews, F. (2020). The COVID-19 pandemic and health inequalities. *Journal of Epidemiology and Community Health, 74*(11), 964–968. https://doi.org/10.1136/jech-2020-214401

Bargh, J. A., & Chartrand, T. L. (1999). The unbearable automaticity of being. *American psychologist*, *54*(7), 462. https://doi.org/10.1037/0003-066X.54.7.462

Barnett, C., Davis, R., Mitchell, C., & Tyson, S. (2022). The vicious cycle of functional neurological disorders: a synthesis of healthcare professionals' views on working with patients with functional neurological disorder. *Disability and rehabilitation*, *44*(10), 1802-1811. https://doi.org/10.1080/09638288.2020.1822935

Barrett, L., Henzi, S. P., & Barton, R. A. (2022). Experts in action: why we need an embodied social brain hypothesis. *Philosophical Transactions of the Royal Society B*, *377*(1844), 20200533. https://doi.org/10.1098/rstb.2020.0533

Barzegaran, E., Carmeli, C., Rossetti, A. O., Frackowiak, R. S., & Knyazeva, M. G. (2016). Weakened functional connectivity in patients with psychogenic non-epileptic seizures (PNES) converges on basal ganglia. *Journal of Neurology, Neurosurgery & Psychiatry*, *87*(3), 332-337. https://doi.org/10.1136/jnnp-2014-309483

Baslet, G., Ehlert, A., Oser, M., & Dworetzky, B. A. (2020). Mindfulness-based therapy for psychogenic nonepileptic seizures. *Epilepsy & Behavior*, *103*, 106534. https://doi.org/10.1016/j.yebeh.2019.106534

Batla, A., Stamelou, M., Edwards, M. J., Pareés, I., Saifee, T. A., Fox, Z., & Bhatia, K. P. (2013). Functional movement disorders are not uncommon in the elderly. *Movement Disorders*, *28*(4), 540-543. https://doi.org/10.1002/mds.25350

Baumeister, D., Akhtar, R., Ciufolini, S., Pariante, C. M., & Mondelli, V. (2016). Childhood trauma and adulthood inflammation: a meta-analysis of peripheral C-reactive protein, interleukin-6 and tumour necrosis factor-α. *Molecular psychiatry*, *21*(5), 642-649. https://doi.org/10.1038/mp.2015.67

Beck, A. T., Steer, R. A., & Brown, G. (1996). Beck depression inventory–II. *Psychological assessment*. https://doi.org/10.1037/t00742-000

Becher, B., Spath, S., & Goverman, J. (2017). Cytokine networks in neuroinflammation. *Nature Reviews Immunology*, *17*(1), 49-59. https://doi.org/10.1038/nri.2016.123

Beedie, C., Terry, P., & Lane, A. (2005). Distinctions between emotion and mood. *Cognition and emotion*, *19*(6), 847-878. https://doi.org/10.1080/02699930541000057

Begley, R., Farrell, L., Lyttle, N., Alty, J., Curran, D., Williams, S., & Graham, C. D. (2023). Clinicians' implicit and explicit attitudes about the legitimacy of functional neurological disorders correlate with referral decisions. *British Journal of Health Psychology*, *28*(2), 604-618. https://doi.org/10.1111/bjhp.12643

Bègue, I., Adams, C., Stone, J., & Perez, D. L. (2019). Structural alterations in functional neurological disorder and related conditions: a software and hardware problem?. *NeuroImage: Clinical*, *22*, 101798. https://doi.org/10.1016/j.nicl.2019.101798

Bègue, I., Blakemore, R., Klug, J., Cojan, Y., Galli, S., Berney, A., ... & Vuilleumier, P. (2018). Metacognition of visuomotor decisions in conversion disorder. *Neuropsychologia*, *114*, 251-265. https://doi.org/10.1016/j.neuropsychologia.2018.04.018

Bennett, D. A. (2001). How can I deal with missing data in my study?. *Australian and New Zealand journal of public health*, *25*(5), 464-469. https://doi.org/10.1111/j.1467-842X.2001.tb00294.x

Bennett, K., Diamond, C., Hoeritzauer, I., Gardiner, P., McWhirter, L., Carson, A., & Stone, J. (2021). A practical review of functional neurological disorder (FND) for the general physician. *Clinical Medicine*, *21*(1), 28. https://doi.org/10.7861/clinmed.2020-0987

Berger, H. (1924). Zur Innervation der Pia mater und der Gehirngefäße. *Archiv Für Psychiatrie Und Nervenkrankheiten*, *70*(1), 216-220. https://doi.org/10.1007/BF01814075

Berger, H. (1929). Über das elektroenkephalogramm des menschen. *Archiv für psychiatrie und nervenkrankheiten*, *87*(1), 527-570. https://doi.org/10.1007/BF01797193

Bernstein, E. M., & Putnam, F. W. (1986). Development, reliability, and validity of a dissociation scale. https://doi.org/10.1037/e609912012-081

Beurel, E., Toups, M., & Nemeroff, C. B. (2020). The bidirectional relationship of depression and inflammation: double trouble. Neuron, 107(2), 234-256. https://doi.org/10.1016/j.neuron.2020.06.002

Bewley, J., Murphy, P. N., Mallows, J., & Baker, G. A. (2005). Does alexithymia differentiate between patients with nonepileptic seizures, patients with epilepsy, and nonpatient controls?. *Epilepsy & Behavior*, *7*(3), 430-437. https://doi.org/10.1016/j.yebeh.2005.06.006

Beydoun, M. A., Obhi, H. K., Weiss, J., Canas, J. A., Beydoun, H. A., Evans, M. K., & Zonderman, A. B. (2020). Systemic inflammation is associated with depressive symptoms differentially by sex and race: a longitudinal study of urban adults. *Molecular psychiatry*, *25*(6), 1286-1300. https://doi.org/10.1038/s41380-019-0408-2

Bhome, R., Huntley, J. D., Price, G., & Howard, R. J. (2019). Clinical presentation and neuropsychological profiles of functional cognitive disorder patients with and without co-morbid depression. *Cognitive neuropsychiatry*, *24*(2), 152-164. https://doi.org/10.1080/13546805.2019.1590190

Binzer, M., Andersen, P. M., & Kullgren, G. (1997). Clinical characteristics of patients with motor disability due to conversion disorder: a prospective control group study. *Journal of Neurology, Neurosurgery & Psychiatry*, *63*(1), 83-88.

Björklund, A. E. (2002). Survey of approaches to improve reliability in LCA. *The international journal of life cycle assessment*, *7*, 64-72. https://doi.org/10.1007/BF02978849

Blakemore, R. L., Sinanaj, I., Galli, S., Aybek, S., & Vuilleumier, P. (2016). Aversive stimuli exacerbate defensive motor behaviour in motor conversion disorder. *Neuropsychologia*, *93*, 229-241. https://doi.org/10.1016/j.neuropsychologia.2016.11.005

Blanco, S. R., Mitra, S., Howard, C. J., & Sumich, A. L. (2023). Psychological trauma, mood and social isolation do not explain elevated dissociation in functional neurological disorder (FND). *Personality and Individual Differences*, *202*, 111952. https://doi.org/10.1016/j.paid.2022.111952

Bob, P., & Mashour, G. A. (2011). Schizophrenia, dissociation, and consciousness. *Consciousness and cognition*, *20*(4), 1042-1049. https://doi.org/10.1016/j.concog.2011.04.013

Boeckle, M., Liegl, G., Jank, R., & Pieh, C. (2016). Neural correlates of conversion disorder: overview and meta-analysis of neuroimaging studies on motor conversion disorder. BMC Psychiatry, 16, 195. doi:10.1186/s12888-016-0890-x https://doi.org/10.1186/s12888-016-0890-x

Boord, P. R., Rennie, C. J., & Williams, L. M. (2007). Integrating" brain" and" body" measures: correlations between EEG and metabolic changes over the human lifespan. *Journal of Integrative Neuroscience*, *6*(01), 205-218. https://doi.org/10.1142/S0219635207001416

Borumandnia, N., Khadembashi, N., Tabatabaei, M., & Alavi Majd, H. (2020). The prevalence rate of sexual violence worldwide: a trend analysis. *BMC public health*, *20*, 1-7. https://doi.org/10.1186/s12889-020-09926-5

Breuer, J., & Freud, S. (1893). On the psychical mechanism of hysterical phenomena. *The standard edition of the complete psychological works of Sigmund Freud*, *2*(1893–5), 1-17.

Briere, J., Dietrich, A., & Semple, R. J. (2016). Dissociative complexity: Antecedents and clinical correlates of a new construct. *Psychological Trauma: Theory, Research, Practice, and Policy*, *8*(5), 577. https://doi.org/10.1037/tra0000126

Briere, J., Weathers, F. W., & Runtz, M. (2005). Is dissociation a multidimensional construct? Data from the Multiscale Dissociation Inventory. *Journal of Traumatic Stress: Official Publication of the International Society for Traumatic Stress Studies*, *18*(3), 221-231. https://doi.org/10.1002/jts.20024

British Psychological Society (2013). Ethics guidelines for internet-mediated research. The British Psychological Society.

Brody, G. H., Yu, T., Chen, Y. F., Kogan, S. M., Evans, G. W., Beach, S. R., ... & Philibert, R. A. (2013). Cumulative socioeconomic status risk, allostatic load, and adjustment: a prospective latent profile analysis with contextual and genetic protective factors. *Developmental psychology*, *49*(5), 913. https://doi.org/10.1037/a0028847

Brown, R. J. (2004). Psychological mechanisms of medically unexplained symptoms: an integrative conceptual model. *Psychological bulletin*, *130*(5), 793-812. https://doi.org/10.1037/0033-2909.130.5.793

Brown, R. J. (2006). Different types of "dissociation" have different psychological mechanisms. *Journal of Trauma & Dissociation*, *7*(4), 7-28. https://doi.org/10.1300/J229v07n04_02

Brown, R. J. (2006). Medically unexplained symptoms: a new model. *Psychiatry*, *5*(2), 43-47. https://doi.org/10.1383/psyt.2006.5.2.43

Brown, R. J. (2016). Dissociation and functional neurologic disorders. *Handbook of clinical neurology*, *139*, 85-94. https://doi.org/10.1016/B978-0-12-801772-2.00008-4

Brown, R. J., & Reuber, M. (2016). Psychological and psychiatric aspects of psychogenic non-epileptic seizures (PNES): a systematic review. *Clinical Psychology Review*, *45*, 157-182. https://doi.org/10.1016/j.cpr.2016.01.003

Brown, R. J., & Reuber, M. (2016). Towards an integrative theory of psychogenic non-epileptic seizures (PNES). *Clinical psychology review*, *47*, 55-70. https://doi.org/10.1016/j.cpr.2016.06.003

Brown, R. J., Bouska, J. F., Frow, A., Kirkby, A., Baker, G. A., Kemp, S., Burness, C., & Reuber, M. (2013). Emotional dysregulation, alexithymia, and attachment in psychogenic nonepileptic seizures. *Epilepsy & Behavior*, *29*(1), 178-183. http://dx.doi.org/10.1016/j.yebeh.2013.07.019

Brown, R. J., Cardeña, E., Nijenhuis, E., Sar, V., & Hart, O. v. de. (2007). Should Conversion Disorder Be Reclassified as a Dissociative Disorder in DSM-V? *Psychosomatics, 48*(5), 369-378. https://doi:10.1176/appi.psy.48.5.369

Bucholz, K. K., Heath, A. C., Reich, T., Hesselbrock, V. M., Nurnberger Jr, J. I., & Schuckit, M. A. (1996). Can we subtype alcoholism? A latent class analysis of data from relatives of alcoholics in a multicenter family study of alcoholism. *Alcoholism: Clinical and Experimental Research*, *20*(8), 1462-1471. https://doi.org/10.1111/j.1530-0277.1996.tb01150.x

Bulloch, A. G., Fiest, K. M., Williams, J. V., Lavorato, D. H., Berzins, S. A., Jetté, N., ... & Patten, S. B. (2015). Depression—a common disorder across a broad spectrum of

neurological conditions: a cross-sectional nationally representative survey. *General hospital psychiatry*, *37*(6), 507-512. https://doi.org/10.1016/j.genhosppsych.2015.06.007

Burgmer, M., Konrad, C., Jansen, A., Kugel, H., Sommer, J., Heindel, W., ... & Knecht, S. (2006). Abnormal brain activation during movement observation in patients with conversion paralysis. *Neuroimage*, *29*(4), 1336-1343. https://doi.org/10.1016/j.neuroimage.2005.08.033

Butler, M., Shipston-Sharman, O., Seynaeve, M., Bao, J., Pick, S., Bradley-Westguard, A., ... & Nicholson, T. (2021). International online survey of 1048 individuals with functional neurological disorder. *European Journal of Neurology*, *28*(11), 3591-3602. https://doi.org/10.1111/ene.15018

Butz, D., & Besio, K. (2009). Autoethnography. *Geography Compass*, *3*(5), 1660-1674. **https://doi.org/10.1111/j.1749-8198.2009.00279.x**

Buzsáki, G., & da Silva, F. L. (2012). High frequency oscillations in the intact brain. *Progress in neurobiology*, *98*(3), 241-249. https://doi.org/10.1016/j.pneurobio.2012.02.004

Buzsáki, G., & Wang, X. J. (2012). Mechanisms of gamma oscillations. *Annual review of neuroscience*, *35*, 203-225. https://doi.org/10.1146/annurev-neuro-062111-150444

Cacioppo, J. T., & Hawkley, L. C. (2003). Social isolation and health, with an emphasis on underlying mechanisms. *Perspectives in biology and medicine*, *46*(3x), S39-S52. https://doi:10.1353/pbm.2003.0063

Cacioppo, J. T., Cacioppo, S., Capitanio, J. P., & Cole, S. W. (2015). The neuroendocrinology of social isolation. *Annual review of psychology*, *66*, 733-767. https://doi.org/10.1146/annurev-psych-010814-015240

Calabresi, P., Galletti, F., Saggese, E., Ghiglieri, V., & Picconi, B. (2007). Neuronal networks and synaptic plasticity in Parkinson's disease: beyond motor deficits. *Parkinsonism & related disorders*, *13*, S259-S262. https://doi.org/10.1016/S1353-8020(08)70013-0

Calsolaro, V., & Edison, P. (2016). Neuroinflammation in Alzheimer's disease: current evidence and future directions. *Alzheimer's & dementia*, *12*(6), 719-732. https://doi.org/10.1016/j.jalz.2016.02.010

Campbell, M. C., Smakowski, A., Rojas-Aguiluz, M., Goldstein, L. H., Cardeña, E., Nicholson, T. R., ... & Pick, S. (2023). Dissociation and its biological and clinical associations in functional neurological disorder: systematic review and meta-analysis. *BJPsych open*, *9*(1), e2. https://doi.org/10.1192/bjo.2022.597

Canavese, C., Ciano, C., Zibordi, F., Zorzi, G., Cavallera, V., & Nardocci, N. (2012). Phenomenology of psychogenic movement disorders in children. *Movement disorders*, *27*(9), 1153-1157. https://doi.org/10.1002/mds.24947

Canna, M., & Seligman, R. (2020). Dealing with the unknown. Functional neurological disorder (FND) and the conversion of cultural meaning. *Social Science & Medicine*, *246*, 112725. https://doi.org/10.1016/j.socscimed.2019.112725

Canu, E., Agosta, F., Tomic, A., Sarasso, E., Petrovic, I., Piramide, N., ... & Filippi, M. (2020). Breakdown of the affective-cognitive network in functional dystonia. *Human Brain Mapping*, *41*(11), 3059-3076. https://doi.org/10.1002/hbm.24997

Cardeña, E., & Carlson, E. (2011). Acute stress disorder revisited. *Annual Review of Clinical Psychology*, *7*, 245-267. https://doi.org/10.1146/annurev-clinpsy-032210-104502

Cardeña, E., & Spiegel, D. (1996). Diagnostic issues, criteria, and comorbidity of dissociative disorders. In *Handbook of dissociation: Theoretical, empirical, and clinical perspectives* (pp. 227-250). Boston, MA: Springer US. https://doi.org/10.1007/978-1-4899-0310-5_11

Carel, H., & Kidd, I. J. (2014). Epistemic injustice in healthcare: A philosophical analysis. *Medicine, Health Care and Philosophy, 17*(4), 529–540. https://doi.org/10.1007/s11019-014-9560-2

Cargo, M., & Mercer, S. L. (2008). The value and challenges of participatory research: Strengthening its practice. *Annual Review of Public Health, 29*, 325–350. https://doi.org/10.1146/annurev.publhealth.29.091307.083824

Carle-Toulemonde, G., Goutte, J., Do-Quang-Cantagrel, N., Mouchabac, S., Joly, C., & Garcin, B. (2023). Overall comorbidities in functional neurological disorder: A narrative review. *L'encephale*. https://doi.org/10.1016/j.encep.2023.06.004

Carle-Toulemonde, G., Goutte, J., Do-Quang-Cantagrel, N., Mouchabac, S., Joly, C., & Garcin, B. (2023). Overall comorbidities in functional neurological disorder: A

narrative review. *L'Encephale*, *49*(4S), S24–S32. https://doi.org/10.1016/j.encep.2023.06.004

Carlozzi, N. E., Tulsky, D. S., & Kisala, P. A. (2011). Traumatic brain injury patient-reported outcome measure: identification of health-related quality-of-life issues relevant to individuals with traumatic brain injury. *Archives of physical medicine and rehabilitation*, *92*(10), S52-S60. https://doi.org/10.1016/j.apmr.2010.12.046

Carlson, E. B., Waelde, L. C., Palmieri, P. A., Macia, K. S., Smith, S. R., & McDade-Montez, E. (2018). Development and validation of the Dissociative Symptoms Scale. *Assessment*, *25*(1), 84-98. https://doi:10.1177/1073191116645904

Carson AL. Epidemiology. In: JS MH, Carson A, eds. Handbook of clinical neurology: functional neurological disorders. Elsevier, 2016: 47–60 https://doi.org/10.1016/B978-0-12-801772-2.00005-9

Carson, A. J., Stone, J., Hansen, C. H., Duncan, R., Cavanagh, J., Matthews, K., Murray, G., & Sharpe, M. (2015). Somatic symptom count scores do not identify patients with symptoms unexplained by disease: a prospective cohort study of neurology outpatients. *Journal of Neurology, Neurosurgery & Psychiatry*, *86*(3), 295-301. https://doi:10.1136/jnnp-2014-308234

Carson, A., Stone, J., Hibberd, C., Murray, G., Duncan, R., & Coleman, R. (2011). Disability, distress and unemployment in neurology outpatients with symptoms 'unexplained by organic disease'. *Journal Of Neurology, Neurosurgery & Psychiatry*, *82*(7), 810-813. https://doi:10.1136/jnnp.2010.220640

Caruana, R., & Niculescu-Mizil, A. (2006, June). An empirical comparison of supervised learning algorithms. In *Proceedings of the 23rd international conference on Machine learning* (pp. 161-168). https://doi.org/10.1145/1143844.1143865

Cassidy, S. A., Bradley, L., Bowen, E., Wigham, S., & Rodgers, J. (2018). Measurement properties of tools used to assess depression in adults with and without autism spectrum conditions: A systematic review. *Autism Research*, *11*(5), 738-754. https://doi.org/10.1002/aur.1922

Castanon, N., Luheshi, G., & Layé, S. (2015). Role of neuroinflammation in the emotional and cognitive alterations displayed by animal models of obesity. *Frontiers in neuroscience*, *9*, 146137. https://doi.org/10.3389/fnins.2015.00229

Castellheim, A., Brekke, O. L., Espevik, T., Harboe, M., & Mollnes, T. (2009). Innate immune responses to danger signals in systemic inflammatory response syndrome and sepsis. *Scandinavian journal of immunology*, *69*(6), 479-491. https://doi.org/10.1111/j.1365-3083.2009.02255.x

Cavicchioli, M., Scalabrini, A., Northoff, G., Mucci, C., Ogliari, A., & Maffei, C. (2021). Dissociation and emotion regulation strategies: A meta-analytic review. *Journal of Psychiatric Research*, *143*, 370-387. https://doi.org/10.1016/j.jpsychires.2021.09.011

Ceylan, M., Yalcin, A., Bayraktutan, O. F., & Laloglu, E. (2018). Serum NT-pro CNP levels in epileptic seizure, psychogenic non-epileptic seizure, and healthy subjects. *Neurological Sciences*, *39*, 2135-2139. https://doi.org/10.1007/s10072-018-3562-4

Clarke, A. R., Barry, R. J., McCarthy, R., & Selikowitz, M. (2001). EEG-defined subtypes of children with attention-deficit/hyperactivity disorder. *Clinical Neurophysiology*, *112*(11), 2098-2105. https://doi.org/10.1016/S1388-2457(01)00668-X

Coebergh, J., Habib, S., Teodoro, T., Edwards, M., & Butler, M. (2024). From Software to Hardware: A Case Series of Functional Neurological Symptoms and Cerebrovascular Disease. *The Journal of Neuropsychiatry and Clinical Neurosciences*, appi-neuropsych. https://doi.org/10.1176/appi.neuropsych.20220182

Cohen, B. H. (2008). *Explaining psychological statistics*. John Wiley & Sons.

Cohen, M. X. (2014). *Analyzing neural time series data: theory and practice*. MIT press. https://doi.org/10.7551/mitpress/9609.001.0001

Cohen, M. X. (2015). Comparison of different spatial transformations applied to EEG data: A case study of error processing. *International Journal of Psychophysiology*, *97*(3), 245-257. https://doi.org/10.1016/j.ijpsycho.2014.09.013

Cohen, S. (1988). Perceived stress in a probability sample of the United States. In S. Spacapan & S. Oskamp (Eds.), *The social psychology of health* (pp. 31–67). Sage Publications, Inc.

Cojan, Y., Waber, L., Carruzzo, A., & Vuilleumier, P. (2009). Motor inhibition in hysterical conversion paralysis. *Neuroimage*, *47*(3), 1026-1037. https://doi.org/10.1016/j.neuroimage.2009.05.023

Cole, R. H., Elmalem, M. S., & Petrochilos, P. (2023). Prevalence of autistic traits in functional neurological disorder and relationship to alexithymia and psychiatric comorbidity. *Journal of the Neurological Sciences*, *446*, 120585. https://doi.org/10.1016/j.jns.2023.120585

Collins, L. M., & Lanza, S. T. (2009). *Latent class and latent transition analysis: With applications in the social, behavioral, and health sciences* (Vol. 718). John Wiley & Sons. https://doi.org/10.1002/9780470567333

Cope, S. R. (2020). EMDR as an Adjunctive Psychological Therapy for Patients With Functional Neurological Disorder: Illustrative Case Examples. *Journal of EMDR Practice and Research, 14*(2), 76-89. https://doi:10.1891/emdr-d-20-00008

Cope, S. R., Smith, J. G., Edwards, M. J., Holt, K., & Agrawal, N. (2021). Enhancing the communication of functional neurological disorder diagnosis: a multidisciplinary education session. *European Journal of Neurology*, *28*(1), 40-47. https://doi.org/10.1111/ene.14525

Costa, P. T., & McCrae, R. R. (2008). The Revised NEO Personality Inventory (NEO-PI-R). *The SAGE Handbook of Personality Theory and Assessment: Volume 2 — Personality Measurement and Testing*, 179-198. https://doi:10.4135/9781849200479.n9

Cotten, S. R., Anderson, W. A., & McCullough, B. M. (2017). Social Isolation Scale. https://doi:10.1037/t62081-000

Cretton, A., Brown, R. J., LaFrance Jr, W. C., & Aybek, S. (2020). What does neuroscience tell us about the conversion model of functional neurological disorders?. *The Journal of neuropsychiatry and clinical neurosciences*, *32*(1), 24-32. https://doi.org/10.1176/appi.neuropsych.19040089

Cromer, L. D., Stevens, C., DePrince, A. P., & Pears, K. (2006). The relationship between executive attention and dissociation in children. Journal of Trauma & Dissociation, 7(4), 135-153. https://doi.org/10.1300/J229v07n04_08

Cronin, E., Brand, B. L., & Mattanah, J. F. (2014). The impact of the therapeutic alliance on treatment outcome in patients with dissociative disorders. *European Journal of Psychotraumatology*, *5*(1), 22676. https://doi.org/10.3402/ejpt.v5.22676

Charcot, J. M. (1888). *Clinical lectures on certain diseases of the nervous system*. Davis.

Charcot, J. M. (1892). *Leçons du mardi à la Salpêtrière* (Vol. 1). Aux Bureau du Progrès Médical.

Charmaz, K. (1991). *Good days, bad days: The self in chronic illness and time*. Rutgers University Press.

Chen, J. E., Lewis, L. D., Chang, C., Tian, Q., Fultz, N. E., Ohringer, N. A., ... & Polimeni, J. R. (2020). Resting-state "physiological networks". *NeuroImage*, *213*, 116707. https://doi.org/10.1016/j.neuroimage.2020.116707

Chen, S. W., Keglovits, M., Devine, M., & Stark, S. (2022). Sociodemographic differences in respondent preferences for survey formats: Sampling bias and potential threats to external validity. *Archives of rehabilitation research and clinical translation*, *4*(1), 100175. https://doi.org/10.1016/j.arrct.2021.100175

Chrousos, G. P. (1995). The hypothalamic–pituitary–adrenal axis and immune-mediated inflammation. *New England Journal of Medicine*, *332*(20), 1351-1363. https://doi.org/10.1056/NEJM199505183322008

Chung, J., Mukerji, S., & Kozlowska, K. (2023). Cortisol and α-amylase awakening response in children and adolescents with functional neurological (conversion) disorder. *Australian & New Zealand Journal of Psychiatry*, *57*(1), 115-129. https://doi.org/10.1177/00048674221082520

Dahlen, A., & Charu, V. (2023). Analysis of Sampling Bias in Large Health Care Claims Databases. *JAMA network open*, *6*(1), e2249804. https://doi.org/10.1001/jamanetworkopen.2022.49804

Dalenberg, C., & Carlson, E. B. (2012). Dissociation in posttraumatic stress disorder part II: How theoretical models fit the empirical evidence and recommendations for modifying

the diagnostic criteria for PTSD. *Psychological Trauma: Theory, Research, Practice, and Policy*, *4*(6), 551-559. https://doi:10.1037/a0027900

D'Alessandro, M., Esteller, R., Vachtsevanos, G., Hinson, A., Echauz, J., & Litt, B. (2003). Epileptic seizure prediction using hybrid feature selection over multiple intracranial EEG electrode contacts: a report of four patients. *IEEE transactions on biomedical engineering*, *50*(5), 603-615. https://doi.org/10.1109/TBME.2003.810706

Damasio, A. R. (2006). *Descartes' error*. Random House.

Dantzer, R. (2012). Depression and inflammation: an intricate relationship. *Biological psychiatry*, *71*(1), 4-5. https://doi.org/10.1016/j.biopsych.2011.10.025

Dantzer, R., & Kelley, K. W. (2007). Twenty years of research on cytokine-induced sickness behavior. *Brain, behavior, and immunity*, *21*(2), 153-160. https://doi.org/10.1016/j.bbi.2006.09.006

Dantzer, R., O'connor, J. C., Freund, G. G., Johnson, R. W., & Kelley, K. W. (2008). From inflammation to sickness and depression: when the immune system subjugates the brain. *Nature reviews neuroscience*, *9*(1), 46-56. https://doi.org/10.1038/nrn2297

Daum, C., Gheorghita, F., Spatola, M., Stojanova, V., Medlin, F., Vingerhoets, F., Berney, A., Gholam-Rezaee, M., Maccaferri, G.E., Hubschmid, M., & Aybek, S. (2015). Interobserver agreement and validity of bedside 'positive signs' for functional weakness, sensory and gait disorders in conversion disorder: a pilot study. *Journal of Neurology, Neurosurgery & Psychiatry, 86*(4), 425-430. https://doi:10.1136/jnnp-2013-307381

Davidson, J. R., T., Tharwani, H. M., & Connor, K. M. (2002). Davidson Trauma Scale (DTS): Normative scores in the general population and effect sizes in placebo-controlled SSRI trials. *Depression and Anxiety, 15*(2), 75-78. https://doi:10.1002/da.10021

Davies, R. D., Gabbert, S. L., & Riggs, P. D. (2001). Anxiety disorders in neurologic illness. *Current Treatment Options in Neurology*, *3*, 333-346. https://doi.org/10.1007/s11940-001-0038-1

De Lange, F. P., Roelofs, K., & Toni, I. (2007). Increased self-monitoring during imagined movements in conversion paralysis. *Neuropsychologia*, *45*(9), 2051-2058. https://doi.org/10.1016/j.neuropsychologia.2007.02.002

De Liège, A., Carle, G., Hingray, C., Lehn, A., Autier, L., Degos, B., & Garcin, B. (2022). Functional neurological disorders in the medical education: an urgent need to fill the gaps. *Revue Neurologique*, *178*(8), 788-795. https://doi.org/10.1016/j.neurol.2022.03.018

de Vroege, L., Khasho, D., Foruz, A., & Van der Feltz-Cornelis, C. M. (2017). Cognitive rehabilitation treatment for mental slowness in conversion disorder: A case report. *Cogent Psychology*, *4*(1), 1348328. https://doi.org/10.1080/23311908.2017.1348328

de Vroege, L., Koppenol, I., Kop, W. J., Riem, M. M., & van der Feltz-Cornelis, C. M. (2021). Neurocognitive functioning in patients with conversion disorder/functional neurological disorder. *Journal of Neuropsychology*, *15*(1), 69-87. https://doi.org/10.1111/jnp.12206

Deeley, Q. (2016). Hypnosis as a model of functional neurologic disorders. *Handbook of clinical neurology*, *139*, 95-103. https://doi.org/10.1016/B978-0-12-801772-2.00009-6

Deka, K., Chaudhury, P. K., Bora, K., & Kalita, P. (2007). A study of clinical correlates and socio-demographic profile in conversion disorder. *Indian journal of psychiatry*, *49*(3), 205-207. https://doi.org/10.4103/0019-5545.37323

Del Giudice, M., & Gangestad, S. W. (2018). Rethinking IL-6 and CRP: Why they are more than inflammatory biomarkers, and why it matters. *Brain, behavior, and immunity*, *70*, 61-75. https://doi.org/10.1016/j.bbi.2018.02.013

del Rio-Casanova, L., González-Vázquez, A. I., Justo, A., Andrade, V., Paramo, M., Brenlla, J., & Blanco-Hortas, A. (2018). The role of emotion dysregulation in Conversion Disorder. *Actas espanolas de psiquiatria*, *46*(Levy, R., & Behrman, J. (1970). Cortical evoked responses in hysterical hemianaesthesia. *Electroencephalography and Clinical Neurophysiology*, *29*(4), 400-402.3), 92-103. https://doi.org/10.1016/0013-4694(70)90048-9

Dell, P. F. (2002). Dissociative phenomenology of dissociative identity disorder. *The Journal of Nervous and Mental Disease*, *190*(1), 10-15. https://doi.org/10.1097/00005053-200201000-00003

Dell, P. F. (2006). The Multidimensional Inventory of Dissociation (MID): A comprehensive measure of pathological dissociation. *Journal of Trauma & Dissociation*, *7*(2), 77-106. https://doi.org/10.1300/J229v07n02_06

Demartini, B., Petrochilos, P., Ricciardi, L., Price, G., Edwards, M. J., & Joyce, E. (2014). The role of alexithymia in the development of functional motor symptoms (conversion disorder). *Journal of Neurology, Neurosurgery & Psychiatry*, *85*(10), 1132-1137. https://doi:10.1136/jnnp-2013-307203

Demartini, B., Ricciardi, L., Crucianelli, L., Fotopoulou, A., & Edwards, M. J. (2016). Sense of body ownership in patients affected by functional motor symptoms (conversion disorder). *Consciousness and cognition*, *39*, 70-76. https://doi:10.1016/j.concog.2015.11.005

Dennis, J. P., & Vander Wal, J. S. (2010). The cognitive flexibility inventory: Instrument development and estimates of reliability and validity. Cognitive therapy and research, 34(3), 241-253. https://doi.org/10.1007/s10608-009-9276-4

Derks, J., Reijneveld, J. C., & Douw, L. (2014). Neural network alterations underlie cognitive deficits in brain tumor patients. *Current opinion in oncology*, *26*(6), 627-633. https://doi.org/10.1097/CCO.0000000000000126

Dhabhar FS. Effects of stress on immune function: the good, the bad, and the beautiful. Immunol Res. 2014 May;58(2-3):193-210. https://doi.org/10.1007/s12026-014-8517-0.PMID:24798553

Dias, S. P., Brouwer, M. C., & van de Beek, D. (2022). Sex and gender differences in bacterial infections. *Infection and Immunity*, *90*(10), e00283-22. https://doi.org/10.1128/iai.00283-22

Diez, I., Larson, A. G., Nakhate, V., Dunn, E. C., Fricchione, G. L., Nicholson, T. R., ... & Perez, D. L. (2021). Early-life trauma endophenotypes and brain circuit–gene expression relationships in functional neurological (conversion) disorder. *Molecular psychiatry*, *26*(8), 3817-3828. https://doi.org/10.1038/s41380-020-0665-0

Diez, I., Williams, B., Kubicki, M., Makris, N., & Perez, D. (2021). Reduced limbic microstructural integrity in functional neurological disorder. *Psychological*

Medicine, 51(3), 485-493. doi:10.1017/S0033291719003386 https://doi.org/10.1017/S0033291719003386

Dinarello, C. A. (1996). Biologic Basis for Interleukin-1 in Disease. *Blood*, *87*(6), 2095-2147. https://doi.org/10.1182/blood.V87.6.2095.bloodjournal8762095

Ding, F., O'Donnell, J., Thrane, A. S., Zeppenfeld, D., Kang, H., Xie, L., ... & Nedergaard, M. (2013). α1-Adrenergic receptors mediate coordinated Ca2+ signaling of cortical astrocytes in awake, behaving mice. *Cell calcium*, *54*(6), 387-394. https://doi.org/10.1016/j.ceca.2013.09.001

DiSabato, D. J., Quan, N., & Godbout, J. P. (2016). Neuroinflammation: the devil is in the details. *Journal of neurochemistry*, *139*, 136-153. https://doi.org/10.1111/jnc.13607

Dosanjh, M., Alty, J., Martin, C., Latchford, G., & Graham, C. D. (2021). What is it like to live with a functional movement disorder? An interpretative phenomenological analysis of illness experiences from symptom onset to post-diagnosis. *British Journal of Health Psychology*, *26*(2), 325-342. https://doi.org/10.1111/bjhp.12478

Dotson, V. M., Levy, S.- A., O'Shea, D. M., McLaren, M. E., & Szymkowicz, S. M. (2020). Assessment of mood disorders in ethnic minorities. In O. Pedraza (Ed.), *Clinical cultural neuroscience: An integrative approach to cross-cultural neuropsychology* (pp. 100–123). Oxford University Press.

Drake, C. E., Codd III, R. T., & Terry, C. (2018). Assessing the validity of implicit and explicit measures of stigma toward clients with substance use disorders among mental health practitioners. *Journal of Contextual Behavioral Science*, *8*, 44-54. https://doi.org/10.1016/j.jcbs.2018.03.005

Drane, D. L., Fani, N., Hallett, M., Khalsa, S. S., Perez, D. L., & Roberts, N. A. (2021). A framework for understanding the pathophysiology of functional neurological disorder. *CNS spectrums*, *26*(6), 555-561. https://doi.org/10.1017/S1092852920001789

Ducroizet, A., Zimianti, I., Golder, D., Hearne, K., Edwards, M., Nielsen, G., & Coebergh, J. (2023). Functional neurological disorder: Clinical manifestations and comorbidities; an online survey. *Journal of Clinical Neuroscience*, *110*, 116-125. https://doi.org/10.1016/j.jocn.2023.02.014

Duncan, R. (2016). Psychogenic nonepileptic seizures: EEG and investigation. Handb Clin Neurol, 139, 305-311. doi:10.1016/b978-0-12-801772-2.00027-8 https://doi.org/10.1016/B978-0-12-801772-2.00027-8

Dunn, E. C., Soare, T. W., Zhu, Y., Simpkin, A. J., Suderman, M. J., Klengel, T., ... & Relton, C. L. (2019). Sensitive periods for the effect of childhood adversity on DNA methylation: results from a prospective, longitudinal study. *Biological psychiatry*, *85*(10), 838-849. https://doi.org/10.1016/j.biopsych.2018.12.023

Duru, O. K., Harawa, N. T., Kermah, D., & Norris, K. C. (2012). Allostatic load burden and racial disparities in mortality. *Journal of the National Medical Association*, *104*(1-2), 89-95. https://doi.org/10.1016/S0027-9684(15)30120-6

Dziak, J. J., Lanza, S. T., & Tan, X. (2014). Effect size, statistical power, and sample size requirements for the bootstrap likelihood ratio test in latent class analysis. *Structural equation modeling: a multidisciplinary journal*, *21*(4), 534-552. https://doi.org/10.1080/10705511.2014.919819

Eaves, L. J., Silberg, J. L., Hewitt, J. K., Rutter, M., Meyer, J. M., Neale, M. C., & Pickles, A. (1993). Analyzing twin resemblance in multisymptom data: genetic applications of a latent class model for symptoms of conduct disorder in juvenile boys. *Behavior Genetics*, *23*, 5-19. https://doi.org/10.1007/BF01067550

Ebner-Priemer, U. W., Badeck, S., Beckmann, C., Wagner, A., Feige, B., Weiss, I., ... & Bohus, M. (2005). Affective dysregulation and dissociative experience in female patients with borderline personality disorder: a startle response study. *Journal of psychiatric research*, *39*(1), 85-92. https://doi.org/10.1016/j.jpsychires.2004.05.001

Edwards, M. J. (2019). Functional neurological disorder: an ethical turning point for neuroscience. *Brain*, *142*(7), 1855-1857. https://doi.org/10.1093/brain/awz194

Edwards, M. J., & Aybek, S. (2020). Gender, Abuse, and Functional Movement Disorders: From His-story to the Future. *Movement disorders clinical practice*, *7*(2), 167. https://doi.org/10.1002/mdc3.12887

Edwards, M. J., Adams, R. A., Brown, H., Pareés, I., & Friston, K. J. (2012). A Bayesian account of 'hysteria'. *Brain*, *135*(11), 3495-3512. https://doi.org/10.1093/brain/aws129

Edwards, M. J., Yogarajah, M., & Stone, J. (2023). Why functional neurological disorder is not feigning or malingering. *Nature Reviews Neurology*, *19*(4), 246-256. https://doi:10.1038/s41582-022-00765-z

Edwards, M., Cope, S. R., & Agrawal, N. (2020). Functional neurological disorders. *Oxford Textbook of Neuropsychiatry*, 267. https://doi.org/10.1093/med/9780198757139.003.0024

Ehring, T., & Watkins, E. R. (2008). Repetitive negative thinking as a transdiagnostic process. *International journal of cognitive therapy*, *1*(3), 192-205. https://doi.org/10.1521/ijct.2008.1.3.192

Ejareh dar, M., & Kanaan, R. A. (2016). Uncovering the etiology of conversion disorder: insights from functional neuroimaging. *Neuropsychiatric disease and treatment*, 143-153. https://doi.org/10.2147/NDT.S65880

Elbers, J., Jaradeh, S., Yeh, A. M., & Golianu, B. (2018). Wired for threat: clinical features of nervous system dysregulation in 80 children. *Pediatric neurology*, *89*, 39-48. https://doi.org/10.1016/j.pediatrneurol.2018.07.007

Elsesser, K., Freyth, C., Lohrmann, T., & Sartory, G. (2008). Startle reactivity and peritraumatic dissociations in acute stress disorder. *Journal of Psychophysiology*, *22*(4), 185-194. https://doi.org/10.1027/0269-8803.22.4.185

Ellenstein, A., Kranick, S. M., & Hallett, M. (2011). An update on psychogenic movement disorders. *Current neurology and neuroscience reports*, *11*, 396-403. https://doi.org/10.1007/s11910-011-0205-z

Ellis, C., Adams, T. E., & Bochner, A. P. (2011). Autoethnography: An overview. *Historical Social Research / Historische Sozialforschung, 36*(4), 273–290. https://www.jstor.org/stable/23032294

Ellis, C., Adams, T. E., & Bochner, A. P. (2011). Autoethnography: An Overview. *Historical Social Research / Historische Sozialforschung*, *36*(4 (138)), 273–290. http://www.jstor.org/stable/23032294

Erickson, K., Drevets, W., & Schulkin, J. (2003). Glucocorticoid regulation of diverse cognitive functions in normal and pathological emotional states. *Neuroscience &*

Biobehavioral Reviews, *27*(3), 233-246. https://doi.org/10.1016/S0149-7634(03)00033-2

Erta, M., Quintana, A., & Hidalgo, J. (2012). Interleukin-6, a major cytokine in the central nervous system. *International journal of biological sciences*, *8*(9), 1254. https://doi.org/10.7150/ijbs.4679

Ertan, D., Aybek, S., LaFrance Jr, W. C., Kanemoto, K., Tarrada, A., Maillard, L., ... & Hingray, C. (2022). Functional (psychogenic non-epileptic/dissociative) seizures: why and how?. *Journal of Neurology, Neurosurgery & Psychiatry*, *93*(2), 144-157. https://doi.org/10.1136/jnnp-2021-326708

Espay, A. J., & Lang, A. E. (2015). Phenotype-specific diagnosis of functional (psychogenic) movement disorders. *Current neurology and neuroscience reports*, *15*, 1-9. https://doi.org/10.1007/s11910-015-0556-y

Espay, A. J., Goldenhar, L. M., Voon, V., Schrag, A., Burton, N., & Lang, A. E. (2009). Opinions and clinical practices related to diagnosing and managing patients with psychogenic movement disorders: an international survey of movement disorder society members. *Movement disorders: Official Journal of the Movement Disorder Society*, *24*(9), 1366-1374. https://doi:10.1002/mds.22618

Espay, A. J., Maloney, T., Vannest, J., Norris, M. M., Eliassen, J. C., Neefus, E., ... & Szaflarski, J. P. (2018). Dysfunction in emotion processing underlies functional (psychogenic) dystonia. *Movement Disorders*, *33*(1), 136-145. https://doi.org/10.1002/mds.27217

Espay, A. J., Ries, S., Maloney, T., Vannest, J., Neefus, E., Dwivedi, A. K., ... & Szaflarski, J. P. (2019). Clinical and neural responses to cognitive behavioral therapy for functional tremor. *Neurology*, *93*(19), e1787-e1798. https://doi.org/10.1212/WNL.0000000000008442

Evans, R. W., & Evans, R. E. (2010). A survey of neurologists on the likeability of headaches and other neurological disorders. *Headache: The Journal of Head and Face Pain*, *50*(7), 1126-1129. https://doi.org/10.1111/j.1526-4610.2010.01708.x

Fabrigar, L. R., Wegener, D. T., MacCallum, R. C., & Strahan, E. J. (1999). Evaluating the use of exploratory factor analysis in psychological research. *Psychological methods*, *4*(3), 272. https://doi.org/10.1037/1082-989X.4.3.272

Factor, S. A., Podskalny, G. D., & Molho, E. S. (1995). Psychogenic movement disorders: frequency, clinical profile, and characteristics. *Journal of Neurology, Neurosurgery & Psychiatry*, *59*(4), 406-412. https://doi.org/10.1136/jnnp.59.4.406

Fagundes, C. P., & Way, B. (2014). Early-life stress and adult inflammation. *Current Directions in Psychological Science*, *23*(4), 277-283. https://doi.org/10.1177/0963721414535603

Fang, C. T., Hsiung, P. C., Yu, C. F., Chen, M. Y., & Wang, J. D. (2002). Validation of the World Health Organization quality of life instrument in patients with HIV infection. *Quality of Life Research*, *11*, 753-762. https://doi.org/10.1023/A:1020870402019

Fargo, J. D., Schefft, B. K., Szaflarski, J. P., Dulay, M. F., Testa, S. M., Privitera, M. D., & Yeh, H. S. (2004). Accuracy of self-reported neuropsychological functioning in individuals with epileptic or psychogenic nonepileptic seizures. *Epilepsy & Behavior*, *5*(2), 143-150. https://doi.org/10.1016/j.yebeh.2003.11.023

Faul, F., Erdfelder, E., Lang, A.-G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods, 39,* 175–191. https://doi.org/10.3758/BF03193146

Faul, L., Knight, L. K., Espay, A. J., Depue, B. E., & LaFaver, K. (2020). Neural activity in functional movement disorders after inpatient rehabilitation. *Psychiatry Research: Neuroimaging*, *303*, 111125. https://doi.org/10.1016/j.pscychresns.2020.111125

Feinstein, A. (2011). Conversion disorder: advances in our understanding. *Cmaj*, *183*(8), 915-920. https://doi.org/10.1503/cmaj.110490

Fekih-Romdhane, F., Jebreen, K., Swaitti, T. *et al.* Validation of the Perceived hope scale in Arabic-speaking adults living in Gaza in the midst of war, destruction and death. *Arch Public Health* **83**, 4 (2025). https://doi.org/10.1186/s13690-024-01494-z

Fend, M., Williams, L., Carson, A. J., & Stone, J. (2020). The Arc de Siècle: functional neurological disorder during the 'forgotten'years of the 20th century. *Brain*, *143*(4), 1278-1284. https://doi.org/10.1093/brain/awaa037

Ferrara, J., & Jankovic, J. (2008). Psychogenic movement disorders in children. *Movement disorders*, *23*(13), 1875-1881. https://doi.org/10.1002/mds.22220

Ferrarese, D., Spagnolo, G., Vecchione, M., Scaldaferri, F., Armuzzi, A., Chieffo, D., ... & Addolorato, G. (2022). Signs of dissociation and symptoms of post-traumatic stress disorder in inflammatory bowel disease: A case-control study. *Digestive Diseases*, *40*(6), 701-709. https://doi.org/10.1159/000521424

Fields, R. D. (2009). *The other brain: From dementia to schizophrenia, how new discoveries about the brain are revolutionizing medicine and science*. Simon and Schuster.

Fiorio, M., Braga, M., Marotta, A., Villa-Sánchez, B., Edwards, M. J., Tinazzi, M., & Barbiani, D. (2022). Functional neurological disorder and placebo and nocebo effects: shared mechanisms. *Nature Reviews Neurology*, *18*(10), 624-635. https://doi.org/10.1038/s41582-022-00711-z

Fobian, A. D., & Elliott, L. (2019). A review of functional neurological symptom disorder etiology and the integrated etiological summary model. *Journal of Psychiatry and Neuroscience*, *44*(1), 8-18. https://doi.org/10.1503/jpn.170190

Fobian, A. D., & Szaflarski, J. P. (2021). Identifying and evaluating novel treatment targets for the development of evidence-based interventions for functional neurological disorder. *Epilepsy & Behavior Reports*, *16*, 100479. https://doi.org/10.1016/j.ebr.2021.100479

Foley, C., Kirkby, A., & Eccles, F. J. (2024). A meta-ethnographic synthesis of the experiences of stigma amongst people with functional neurological disorder. *Disability and Rehabilitation*, *46*(1), 1-12. https://doi.org/10.1080/09638288.2022.2155714

Folks, D. G., Ford, C. V., & Regan, W. M. (1984). Conversion symptoms in a general hospital. *Psychosomatics*, *25*(4), 285-295. https://doi.org/10.1016/S0033-3182(84)73046-5

Fonseca, L. C., Tedrus, G. M., Rezende, A. L. R., & Giordano, H. F. (2015). Coherence of brain electrical activity: a quality of life indicator in Alzheimer's disease? Coerência da

atividade elétrica cerebral: indicador da qualidade de vida na doença de Alzheimer?. *Arquivos de Neuro-psiquiatria*, *73*, 396-401. https://doi.org/10.1590/0004-282X20150035

Forejtová, Z., Serranová, T., Sieger, T., Slovák, M., Nováková, L., Věchetová, G., ... & Edwards, M. J. (2023). The complex syndrome of functional neurological disorder. *Psychological Medicine*, *53*(7), 3157-3167. https://doi.org/10.1017/S0033291721005225

Forkmann, T., Spangenberg, L., Rath, D., Hallensleben, N., Hegerl, U., Kersting, A., & Glaesmer, H. (2018). Assessing suicidality in real time: A psychometric evaluation of self-report items for the assessment of suicidal ideation and its proximal risk factors using ecological momentary assessments. *Journal of abnormal psychology*, *127*(8), 758. https://doi.org/10.1037/abn0000381

Foroughi, A. A., Nazeri, M., & Asadi-Pooya, A. A. (2020). Brain connectivity abnormalities in patients with functional (psychogenic nonepileptic) seizures: A systematic review. *Seizure*, *81*, 269-275. https://doi.org/10.1016/j.seizure.2020.08.024

Frank, A. W. (2013). *The wounded storyteller: Body, illness, and ethics* (2nd ed.). University of Chicago Press.

Frank, A. W. (2016). From sick role to narrative subject: An analytic memoir. *Health, 20*(1), 9–21. https://doi.org/10.1177/1363459315617312

Frank, M. G., Weber, M. D., Watkins, L. R., & Maier, S. F. (2016). Stress-induced neuroinflammatory priming: a liability factor in the etiology of psychiatric disorders. *Neurobiology of stress*, *4*, 62-70. https://doi.org/10.1016/j.ynstr.2015.12.004

Frauscher, B., von Ellenrieder, N., Ferrari-Marinho, T., Avoli, M., Dubeau, F., & Gotman, J. (2015). Facilitation of epileptic activity during sleep is mediated by high amplitude slow waves. *Brain*, *138*(6), 1629-1641. https://doi.org/10.1093/brain/awv073

Frewen, P. A., & Lanius, R. A. (2006). Neurobiology of dissociation: Unity and disunity in mind–body–brain. *Psychiatric Clinics*, *29*(1), 113-128. https://doi.org/10.1016/j.psc.2005.10.016

Fricker, M. (2007). *Epistemic injustice: Power and the ethics of knowing*. Oxford University Press. https://doi.org/10.1093/acprof:oso/9780198237907.001.0001

Gabay, C., & Kushner, I. (1999). Acute-phase proteins and other systemic responses to inflammation. *New England journal of medicine*, *340*(6), 448-454. https://doi.org/10.1056/NEJM199902113400607

Gary, F. A., Yarandi, H., Evans, E., Still, C., Mickels, P., Hassan, M., Campbell, D., & Conic, R. (2018). Beck Depression Inventory-II: Factor Analyses with Three Groups of Midlife Women of African Descent in the Midwest, the South, and the U.S. Virgin Islands. *Issues in mental health nursing*, *39*(3), 233–243. https://doi.org/10.1080/01612840.2017.1373175

Gebrie, M. H. (2018). An analysis of beck depression inventory 2nd edition (BDI-II). *Global Journal of Endocrinological Metabolism*, *2*(3), 1-5.

Gelauff, J. M., Kingma, E. M., Kalkman, J. S., Bezemer, R., van Engelen, B. G. M., Stone, J., Tijssen, M. A., & Rosmalen, J. G. (2018). Fatigue, not self-rated motor symptom severity, affects quality of life in functional motor disorders. *Journal of neurology*, *265*, 1803-1809. https://doi.org/10.1007/s00415-018-8915-7

Gelauff, J. M., Rosmalen, J. G. M., Gardien, J., Stone, J., & Tijssen, M. A. J. (2020). Shared demographics and comorbidities in different functional motor disorders. *Parkinsonism & Related Disorders*, *70*, 1-6. https://doi.org/10.1016/j.parkreldis.2019.11.018

Gelauff, J., & Stone, J. (2016). Prognosis of functional neurologic disorders. *Handbook of clinical neurology*, *139*, 523-541. https://doi.org/10.1016/B978-0-12-801772-2.00043-6

Gelauff, J., Stone, J., Edwards, M., & Carson, A. (2014). The prognosis of functional (psychogenic) motor symptoms: a systematic review. *Journal of Neurology, Neurosurgery & Psychiatry*, *85*(2), 220-226. https://doi.org/10.1136/jnnp-2013-305321

Geroin, C., Stone, J., Camozzi, S., Demartini, B., Gandolfi, M., & Tinazzi, M. (2022). Triggers in functional motor disorder: a clinical feature distinct from precipitating factors. *Journal of neurology*, *269*(7), 3892-3898. https://doi.org/10.1007/s00415-022-11102-1

Ghahramani, Z. (2015). Probabilistic machine learning and artificial intelligence. *Nature*, *521*(7553), 452-459. https://doi.org/10.1038/nature14541

Gholami Doborjeh, Z., Kasabov, N., Gholami Doborjeh, M., & Sumich, A. (2018). Modelling peri-perceptual brain processes in a deep learning spiking neural network architecture. *Scientific reports*, *8*(1), 8912. https://doi.org/10.1038/s41598-018-27169-8

Giacometti, P., Perdue, K. L., & Diamond, S. G. (2014). Algorithm to find high density EEG scalp coordinates and analysis of their correspondence to structural and functional regions of the brain. *Journal of neuroscience methods*, *229*, 84-96. https://doi.org/10.1016/j.jneumeth.2014.04.020

Gibbs, G. (1988). *Learning by doing: A guide to teaching and learning methods.* Oxford Polytechnic.

Gilmartin, H. M., Grota, P. G., & Sousa, K. (2013,). Isolation: a concept analysis. In *Nursing Forum*, 48(1), pp. 54-60). https://doi.org/10.1111/nuf.12001

Glaser, R., & Kiecolt-Glaser, J. K. (2005). Stress-induced immune dysfunction: implications for health. *Nature reviews immunology*, *5*(3), 243-251. https://doi.org/10.1038/nri1571

Glass, S. P., Matin, N., Williams, B., Mello, J., Stephen, C. D., Young, S. S., Callahan, J., LaFrance, W. C., & Perez, D. L. (2018). Neuropsychiatric factors linked to adherence and short-term outcome in a US functional neurological disorders clinic: a retrospective cohort study. *The Journal of neuropsychiatry and clinical neurosciences*, *30*(2), 152-159. https://doi.org/10.1176/appi.neuropsych.17060117

Gleick, J. (1987). The butterfly effect. *Chaos: Making a New Science*, 9-32.

Gleick, J. (2008). *Chaos: Making a new science*. Penguin.

Gloster, A. T., Rhoades, H. M., Novy, D., Klotsche, J., Senior, A., Kunik, M., Wilson, N., & Stanley, M. A. (2008). Psychometric properties of the Depression Anxiety and Stress Scale-21 in older primary care patients. *Journal of affective disorders*, *110*(3), 248–259. https://doi.org/10.1016/j.jad.2008.01.023

Goldberg, P. (2020). Body-mind dissociation, altered states, and alter worlds. *Journal of the American Psychoanalytic Association*, *68*(5), 769-806. https://doi.org/10.1177/0003065120968422

Goldstein, L. H., & Mellers, J. D. C. (2006). Ictal symptoms of anxiety, avoidance behaviour, and dissociation in patients with dissociative seizures. *Journal of Neurology, Neurosurgery & Psychiatry*, *77*(5), 616-621. https://doi:10.1136/jnnp.2005.066878

Goldstein, L. H., Robinson, E. J., Reuber, M., Chalder, T., Callaghan, H., Eastwood, C., ... & Samarasekera, S. (2019). Characteristics of 698 patients with dissociative seizures: a UK multicenter study. *Epilepsia*, *60*(11), 2182-2193. https://doi.org/10.1111/epi.16350

Gorostowicz, A., Rizvi, S. J., Kennedy, S. H., Chrobak, A. A., Dudek, D., Cyranka, K., ... & Siwek, M. (2023). Polish adaptation of the Dimensional Anhedonia Rating Scale (DARS)-validation in the clinical sample. *Frontiers in Psychiatry*, *14*, 1268290. https://doi.org/10.3389/fpsyt.2023.1268290

Graham, C. D., O'Hara, D. J., & Kemp, S. (2018). A case series of Acceptance and Commitment Therapy (ACT) for reducing symptom interference in functional neurological disorders. *Clinical psychology & psychotherapy*, *25*(3), 489-496. https://doi.org/10.1002/cpp.2174

Grant, B., Burgen, B., & Kearns, R. (2004). Idealism and the reality of the PhD process. *Gender, Work & Organization, 11*(2), 174–185. https://doi.org/10.1111/j.1468-0432.2004.00227.x

Grassi-Oliveira, R., Ashy, M., & Stein, L. M. (2008). Psychobiology of childhood maltreatment: effects of allostatic load?. *Brazilian Journal of Psychiatry*, *30*, 60-68. https://doi.org/10.1590/S1516-44462008000100012

Greenhalgh, T. (2016). *Cultural contexts of health: The use of narrative research in the health sector*. World Health Organization. https://apps.who.int/iris/handle/10665/326460

Greenhalgh, T., Fisman, D., & Cane, D. J. (2020). Adaptation and crisis: Rethinking research methodologies in the age of pandemics. *Social Science & Medicine, 260*, 113201. https://doi.org/10.1016/j.socscimed.2020.113201

Greenhalgh, T., Jackson, C., Shaw, S., & Janamian, T. (2016). Achieving research impact through co-creation in community-based health services: Literature review and case study. *The Milbank Quarterly, 94*(2), 392–429. https://doi.org/10.1111/1468-0009.12197

Greenland, S., Pearl, J., & Robins, J. M. (1999). Confounding and collapsibility in causal inference. *Statistical science*, *14*(1), 29-46. https://doi.org/10.1214/ss/1009211805

Griesbach, G. S., Masel, B. E., Helvie, R. E., & Ashley, M. J. (2018). The impact of traumatic brain injury on later life: effects on normal aging and neurodegenerative diseases. *Journal of neurotrauma*, *35*(1), 17-24. https://doi.org/10.1089/neu.2017.5103

Grof, P. (2002). Mood disorders—new definitions, treatment directions, and understanding. *The Canadian Journal of Psychiatry*, *47*(2), 123-124. https://doi.org/10.1177/070674370204700201

Grothe, K. B., Dutton, G. R., Jones, G. N., Bodenlos, J., Ancona, M., & Brantley, P. J. (2005). Validation of the Beck Depression Inventory-II in a low-income African American sample of medical outpatients. *Psychological assessment*, *17*(1), 110 - 114. https://doi.org/10.1037/1040-3590.17.1.110

Gruol, D. L. (2015). IL-6 regulation of synaptic function in the CNS. *Neuropharmacology*, *96*, 42-54. https://doi.org/10.1016/j.neuropharm.2014.10.023

Guenther, L., Leber, S., & Schnell, T. (2021). "I have to work twice as hard" – Single mothers in academia and their experiences with work-life balance. *Higher Education Research & Development, 40*(2), 304–317. https://doi.org/10.1080/07294360.2020.1852188

Guidi, J., Lucente, M., Sonino, N., & Fava, G. A. (2020). Allostatic load and its impact on health: a systematic review. *Psychotherapy and psychosomatics*, *90*(1), 11-27. https://doi.org/10.1159/000510696

Guilcher, S. J. T., Catharine Craven, B., Bassett-Gunter, R. L., Cimino, S. R., & Hitzig, S. L. (2021). An examination of objective social disconnectedness and perceived social isolation among persons with spinal cord injury/dysfunction: a descriptive cross-sectional study. *Disability and Rehabilitation, 43*(1), 69-75. https://doi:10.1080/09638288.2019.1616328

Gulpek, D., Kelemence Kaplan, F., Kesebir, S., & Bora, O. (2014). Alexithymia in patients with conversion disorder. *Nordic journal of psychiatry*, *68*(5), 300-305. https://doi.org/10.3109/08039488.2013.814711

Gupta, A., & Lang, A. E. (2009). Psychogenic movement disorders. *Current opinion in neurology*, *22*(4), 430-436. https://doi.org/10.1097/WCO.0b013e32832dc169

Guralnik, O., Giesbrecht, T., Knutelska, M., Sirroff, B., & Simeon, D. (2007). Cognitive functioning in depersonalization disorder. *The Journal of nervous and mental disease*, *195*(12), 983-988. https://doi.org/10.1097/NMD.0b013e31815c19cd

Hagenaars, J. A., & McCutcheon, A. L. (Eds.). (2002). *Applied latent class analysis*. Cambridge University Press. https://doi.org/10.1017/CBO9780511499531

Hagmann, P., Cammoun, L., Gigandet, X., Meuli, R., Honey, C. J., Wedeen, V. J., & Sporns, O. (2008). Mapping the structural core of human cerebral cortex. *PLoS biology*, *6*(7), e159. https://doi.org/10.1371/journal.pbio.0060159

Hahs-Vaughn, D. L. (2016). *Applied multivariate statistical concepts*. Routledge. https://doi.org/10.4324/9781315816685

Halvorsen, J. Ø., Stenmark, H., Neuner, F., & Nordahl, H. M. (2014). Does dissociation moderate treatment outcomes of narrative exposure therapy for PTSD? A secondary analysis from a randomized controlled clinical trial. *Behaviour Research and Therapy*, *57*, 21-28. https://doi.org/10.1016/j.brat.2014.03.010

Hall, W. J., Chapman, M. V., Lee, K. M., Merino, Y. M., Thomas, T. W., Payne, B. K., ... & Coyne-Beasley, T. (2015). Implicit racial/ethnic bias among health care professionals and its influence on health care outcomes: a systematic review. *American journal of public health*, *105*(12), e60-e76. https://doi.org/10.2105/AJPH.2015.302903a

Hallett, M. (2006). Psychogenic movement disorders: a crisis for neurology. *Current neurology and neuroscience reports*, *6*(4), 269-271. https://doi.org/10.1007/s11910-006-0015-x

Hallett, M., Aybek, S., Dworetzky, B. A., McWhirter, L., Staab, J. P., & Stone, J. (2022). Functional neurological disorder: new subtypes and shared mechanisms. *The Lancet Neurology*, *21*(6), 537-550. https://doi.org/10.1016/S1474-4422(21)00422-1

Haraway, D. J. (1988). Situated knowledges: The science question in feminism and the privilege of partial perspective. *Feminist Studies, 14*(3), 575–599. https://doi.org/10.2307/3178066

Harding, S. (1991). *Whose science? Whose knowledge? Thinking from women's lives*. Cornell University Press.

Hassa, T., Sebastian, A., Liepert, J., Weiller, C., Schmidt, R., & Tüscher, O. (2017). Symptom-specific amygdala hyperactivity modulates motor control network in conversion disorder. *NeuroImage: Clinical*, *15*, 143-150. https://doi.org/10.1016/j.nicl.2017.04.004

Hassa, T., Spiteri, S., Schmidt, R., Merkel, C., & Schoenfeld, M. A. (2021). Increased amygdala activity associated with cognitive reappraisal strategy in functional neurologic disorder. *Frontiers in Psychiatry*, *12*, 613156. https://doi.org/10.3389/fpsyt.2021.613156

Hébert, M., Lavoie, F., & Blais, M. (2014). Post Traumatic Stress Disorder/PTSD in adolescent victims of sexual abuse: resilience and social support as protection factors. *Ciencia & saude coletiva*, *19*, 685-694. https://doi.org/10.1590/1413-81232014193.15972013

Henry, J. D., & Crawford, J. R. (2005). The short-form version of the Depression Anxiety Stress Scales (DASS-21): Construct validity and normative data in a large non-clinical sample. *British journal of clinical psychology*, *44*(2), 227-239. https://doi.org/10.1348/014466505X29657

Herbert, B. M., Herbert, C., & Pollatos, O. (2011). On the relationship between interoceptive awareness and alexithymia: is interoceptive awareness related to emotional awareness?. *Journal of personality*, *79*(5), 1149-1175. https://doi.org/10.1111/j.1467-6494.2011.00717.x

Herbert, L. D., Kim, R., Hassan, A. A., Wilkinson-Smith, A., & Waugh, J. L. (2021). When neurologists diagnose functional neurological disorder, why don't they code for it?. *CNS spectrums*, *26*(6), 664-674. https://doi.org/10.1017/S1092852921000833

Hermans, E. J., Van Marle, H. J., Ossewaarde, L., Henckens, M. J., Qin, S., Van Kesteren, M. T., ... & Fernández, G. (2011). Stress-related noradrenergic activity prompts large-scale neural network reconfiguration. *science*, *334*(6059), Frauscher, B., von Ellenrieder, N., Zelmann, R., Rogers, C., Nguyen, D. K., Kahane, P., ... & Gotman, J. (2018). High-frequency oscillations in the normal human brain. *Annals of neurology*, *84*(3), 374-385.1151-1153. https://doi.org/10.1126/science.1209603

Herrmann, C. S., & Demiralp, T. (2005). Human EEG gamma oscillations in neuropsychiatric disorders. *Clinical neurophysiology*, *116*(12), 2719-2733. https://doi.org/10.1016/j.clinph.2005.07.007

Hickie, I., Lloyd, A., Hadzi-Pavlovic, D., Parker, G., Bird, K., & Wakefield, D. (1995). Can the chronic fatigue syndrome be defined by distinct clinical features?. *Psychological medicine*, *25*(5), 925-935. https://doi.org/10.1017/S0033291700037417

Hingray, C., Ertan, D., Reuber, M., Lother, A. S., Chrusciel, J., Tarrada, A., ... & El-Hage, W. (2022). Heterogeneity of patients with functional/dissociative seizures: Three multidimensional profiles. *Epilepsia*, *63*(6), 1500-1515. https://doi.org/10.1111/epi.17230

Holden, J. S. (2013). *Development and psychometric properties of the Dissociative Continuum Scale-II (DCS-II)*. Alliant International University.

Holmes, E. A., Brown, R. J., Mansell, W., Fearon, R. P., Hunter, E. C., Frasquilho, F., & Oakley, D. A. (2005). Are there two qualitatively distinct forms of dissociation? A review and some clinical implications. *Clinical psychology review*, *25*(1), 1-23. https://doi.org/10.1016/j.cpr.2004.08.006

Holmes, E. A., Brown, R. J., Mansell, W., Fearon, R. P., Hunter, E. C., Frasquilho, F., & Oakley, D. A. (2005). Are there two qualitatively distinct forms of dissociation? A review and some clinical implications. *Clinical psychology review*, *25*(1), 1-23. https://doi:10.1016/j.cpr.2004.08.006

Holland, L. S. H., & Smith, S. (1855). *A memoir of the Reverend Sydney Smith* (Vol. 2). Harper & Brothers.

Hori, H., & Kim, Y. (2019). Inflammation and post-traumatic stress disorder. *Psychiatry and clinical neurosciences*, *73*(4), 143-153. https://doi.org/10.1111/pcn.12820

Howell, D. C. (2012). *Statistical methods for psychology*. Cengage Learning.

Howren, M. B., Lamkin, D. M., & Suls, J. (2009). Associations of depression with C-reactive protein, IL-1, and IL-6: a meta-analysis. *Psychosomatic medicine*, *71*(2), 171-186. https://doi.org/10.1097/PSY.0b013e3181907c1b

Huang, R. C., Lillycrop, K. A., Beilin, L. J., Godfrey, K. M., Anderson, D., Mori, T. A., ... & Melton, P. E. (2019). Epigenetic age acceleration in adolescence associates with BMI, inflammation, and risk score for middle age cardiovascular disease. *The Journal of Clinical Endocrinology & Metabolism*, *104*(7), 3012-3024. https://doi.org/10.1210/jc.2018-02076

Hudson, S. (2020). How people develop functional neurological disorder: Some current theories. *British Journal of Neuroscience Nursing*, *16*(2), 69-72. https://doi.org/10.12968/bjnn.2020.16.2.69

Hunter, E. C. M., Phillips, M. L., Chalder, T., Sierra, M., & David, A. S. (2003). Depersonalisation disorder: a cognitive–behavioural conceptualisation. *Behaviour Research and Therapy*, *41*(12), 1451-1467. https://doi.org/10.1016/S0005-7967(03)00066-4

Indiveri, G., Corradi, F., & Qiao, N. (2015, December). Neuromorphic architectures for spiking deep neural networks. In *2015 IEEE International Electron Devices Meeting (IEDM)* (pp. 4-2). IEEE. https://doi.org/10.1109/IEDM.2015.7409623

Ingersoll, M. A. (2017). Sex differences shape the response to infectious diseases. *PLoS pathogens*, *13*(12), e1006688. https://doi.org/10.1371/journal.ppat.1006688

Izadyar, S., Shah, V., & James, B. (2018). Comparison of postictal semiology and behavior in psychogenic nonepileptic and epileptic seizures. *Epilepsy & Behavior*, *88*, 123-129. https://doi.org/10.1016/j.yebeh.2018.08.020

Janet, P. (1907). The major symptoms of hysteria: Fifteen lectures given in the medical school of Harvard University. *Macmillan*. https://doi.org/10.1037/10008-000

Janiri, D., Moccia, L., Dattoli, L., Pepe, M., Molinaro, M., De Martin, V., ... & Sani, G. (2021). Emotional dysregulation mediates the impact of childhood trauma on psychological distress: First Italian data during the early phase of COVID-19 outbreak. *Australian & New Zealand Journal of Psychiatry*, *55*(11), 1071-1078. https://doi.org/10.1177/0004867421998802

Jeffirs, Stephanie & Petri, Jessica & Camden, Abigail & Jackson, Brianna & Weathers, Frank. (2023). Psychometric Evaluation of the Multiscale Dissociation Inventory (MDI): A Replication and Extension in Two Trauma-Exposed Samples. European Journal of Trauma & Dissociation. 7. https://doi.org/100324.10.1016/j.ejtd.2023.100324

Ji, R. R., Chamessian, A., & Zhang, Y. Q. (2016). Pain regulation by non-neuronal cells and inflammation. *Science*, *354*(6312), 572-577. https://doi.org/10.1126/science.aaf8924

Johnco, C., Wuthrich, V. M., & Rapee, R. M. (2014). Reliability and validity of two self-report measures of cognitive flexibility. *Psychological Assessment, 26*(4), 1381–1387. https://doi.org/10.1037/a0038009

Jones, B., Reuber, M., & Norman, P. (2016). Correlates of health-related quality of life in adults with psychogenic nonepileptic seizures: a systematic review. *Epilepsia*, *57*(2), 171-181. https://doi.org/10.1111/epi.13268

Jorge, R. E. (2015). Mood disorders. *Handbook of clinical neurology*, *128*, 613-631. https://doi.org/10.1016/B978-0-444-63521-1.00038-8

Jungilligens, J., Paredes-Echeverri, S., Popkirov, S., Barrett, L. F., & Perez, D. L. (2022). A new science of emotion: implications for functional neurological disorder. *Brain*, *145*(8), 2648-2663. https://doi.org/10.1093/brain/awac204

Jungilligens, J., Wellmer, J., Schlegel, U., Kessler, H., Axmacher, N., & Popkirov, S. (2020). Impaired emotional and behavioural awareness and control in patients with dissociative seizures. *Psychological Medicine*, *50*(16), 2731-2739. https://doi.org/10.1017/S0033291719002861

Kafer, A. (2013). *Feminist, queer, crip*. Indiana University Press. https://iupress.org/9780253009340/feminist-queer-crip/

Kanaan, R. A., & Craig, T. K. (2019). Conversion disorder and the trouble with trauma. *Psychological medicine*, *49*(10), 1585-1588. https://doi.org/10.1017/S0033291719000990

Kanaan, R. A., Armstrong, D., & Wessely, S. C. (2011). Neurologists' understanding and management of conversion disorder. *Journal of Neurology, Neurosurgery & Psychiatry*, *82*(9), 961-966. https://doi.org/10.1136/jnnp.2010.233114

Kaplan, M. J., Dwivedi, A. K., Privitera, M. D., Isaacs, K., Hughes, C., & Bowman, M. (2013). Comparisons of childhood trauma, alexithymia, and defensive styles in patients with psychogenic non-epileptic seizures vs. epilepsy: implications for the etiology of conversion disorder. *Journal of Psychosomatic Research*, *75*(2), 142-146. https://doi.org/10.1016/j.jpsychores.2013.06.005

Karatzias, T., Shevlin, M., Fyvie, C., Hyland, P., Efthymiadou, E., Wilson, D., ... & Cloitre, M. (2017). Evidence of distinct profiles of posttraumatic stress disorder (PTSD) and

complex posttraumatic stress disorder (CPTSD) based on the new ICD-11 trauma questionnaire (ICD-TQ). *Journal of affective disorders*, *207*, 181-187. https://doi.org/10.1016/j.jad.2016.09.032

Karpova, N. N. (2014). Role of BDNF epigenetics in activity-dependent neuronal plasticity. *Neuropharmacology*, *76*, 709-718. https://doi.org/10.1016/j.neuropharm.2013.04.002

Kasabov, N. K. (2019). *Time-space, spiking neural networks and brain-inspired artificial intelligence*. Berlin, Heidelberg: Springer Berlin Heidelberg. https://doi.org/10.1007/978-3-662-57715-8

Katrinli, S., Oliveira, N. C., Felger, J. C., Michopoulos, V., & Smith, A. K. (2022). The role of the immune system in posttraumatic stress disorder. *Translational Psychiatry*, *12*(1), 313. https://doi.org/10.1038/s41398-022-02094-7

Katsu, Y., & Baker, M. E. (2021). Cortisol. In *Handbook of hormones* (pp. 947-949). Academic Press. https://doi.org/10.1016/B978-0-12-820649-2.00261-8

Kauhanen, J., Kaplan, G. A., Julkunen, J., Wilson, T. W., & Salonen, J. T. (1993). Social factors in alexithymia. *Comprehensive psychiatry*, *34*(5), 330-335. https://doi.org/10.1016/0010-440X(93)90019-Z

Keil, A., Debener, S., Gratton, G., Junghöfer, M., Kappenman, E. S., Luck, S. J., ... & Yee, C. M. (2014). Committee report: publication guidelines and recommendations for studies using electroencephalography and magnetoencephalography. *Psychophysiology*, *51*(1), 1-21. https://doi.org/10.1111/psyp.12147

Kemp, S., Kapur, N., Graham, C. D., & Reuber, M. (2022). Functional cognitive disorder: differential diagnosis of common clinical presentations. *Archives of Clinical Neuropsychology*, *37*(6), 1158-1176. https://doi.org/10.1093/arclin/acac020

Kernick, D. (2005). Migraine—new perspectives from chaos theory. *Cephalalgia*, *25*(8), 561-566. https://doi.org/10.1111/j.1468-2982.2005.00934.x

Kerr, W. T., Janio, E. A., Le, J. M., Hori, J. M., Patel, A. B., Gallardo, N. L., ... & Stern, J. M. (2016). Diagnostic delay in psychogenic seizures and the association with anti-seizure medication trials. *Seizure*, *40*, 123-126. https://doi.org/10.1016/j.seizure.2016.06.015

Kever, A., Pollatos, O., Vermeulen, N., & Grynberg, D. (2015). Interoceptive sensitivity facilitates both antecedent-and response-focused emotion regulation strategies. *Personality and Individual Differences*, *87*, 20-23. https://doi.org/10.1016/j.paid.2015.07.014

Keynejad, R. C., Carson, A. J., David, A. S., & Nicholson, T. R. (2017). Functional neurological disorder: psychiatry's blind spot. *The Lancet Psychiatry*, *4*(3), e2-e3. https://doi.org/10.1016/S2215-0366(17)30036-6

Keynejad, R. C., Frodl, T., Kanaan, R., Pariante, C., Reuber, M., & Nicholson, T. R. (2019). Stress and functional neurological disorders: mechanistic insights. *Journal of Neurology, Neurosurgery & Psychiatry*, *90*(7), 813-821. https://doi.org/10.1136/jnnp-2018-318297

Khera, A., McGuire, D. K., Murphy, S. A., Stanek, H. G., Das, S. R., Vongpatanasin, W., ... & de Lemos, J. A. (2005). Race and gender differences in C-reactive protein levels. *Journal of the American college of cardiology*, *46*(3), 464-469. https://doi.org/10.1016/j.jacc.2005.04.051

Kiecolt-Glaser, J. K., Derry, H. M., & Fagundes, C. P. (2015). Inflammation: depression fans the flames and feasts on the heat. *American Journal of Psychiatry*, *172*(11), 1075-1091. https://doi.org/10.1176/appi.ajp.2015.15020152

Kienle, J., Rockstroh, B., Bohus, M., Fiess, J., Huffziger, S., & Steffen-Klatt, A. (2017). Somatoform dissociation and posttraumatic stress syndrome–two sides of the same medal? A comparison of symptom profiles, trauma history and altered affect regulation between patients with functional neurological symptoms and patients with PTSD. *BMC psychiatry*, *17*, 1-11. https://doi.org/10.1186/s12888-017-1414-z

Kienle, J., Rockstroh, B., Fiess, J., Schmidt, R., Popov, T., & Steffen-Klatt, A. (2018). Variation of functional neurological symptoms and emotion regulation with time. *Frontiers in Psychiatry*, *9*, 330035. https://doi.org/10.3389/fpsyt.2018.00035

Kim, D., Kim, M. A., Cho, I. H., Kim, M. S., Lee, S., Jo, E. K., ... & Lee, S. J. (2007). A critical role of toll-like receptor 2 in nerve injury-induced spinal cord glial cell activation and pain hypersensitivity. *Journal of Biological Chemistry*, *282*(20), 14975-14983. https://doi.org/10.1074/jbc.M607277200

Kleckner, I. R., Zhang, J., Touroutoglou, A., Chanes, L., Xia, C., Simmons, W. K., ... & Feldman Barrett, L. (2017). Evidence for a large-scale brain system supporting allostasis and interoception in humans. *Nature human behaviour*, *1*(5), 0069. https://doi.org/10.1038/s41562-017-0069

Knyazev, G. G. (2012). EEG delta oscillations as a correlate of basic homeostatic and motivational processes. *Neuroscience & Biobehavioral Reviews*, *36*(1), 677-695. https://doi.org/10.1016/j.neubiorev.2011.10.002

Knyazev, G. G., Savostyanov, A. N., Bocharov, A. V., Slobodskaya, H. R., Bairova, N. B., Tamozhnikov, S. S., & Stepanova, V. V. (2017). Effortful control and resting state networks: a longitudinal EEG study. *Neuroscience*, *346*, 365-381. https://doi.org/10.1016/j.neuroscience.2017.01.031

Kocalevent, RD., Berg, L., Beutel, M.E. *et al.* Social support in the general population: standardization of the Oslo social support scale (OSSS-3). *BMC Psychol* **6**, 31 (2018). https://doi.org/10.1186/s40359-018-0249-9

Kola, S., & LaFaver, K. (2022). Functional movement disorder and functional seizures: What have we learned from different subtypes of functional neurological disorders?. *Epilepsy & Behavior Reports*, *18*, 100510. https://doi.org/10.1016/j.ebr.2021.100510

Kolozsvári, L. R., Rekenyi, V., Garbóczy, S., Hőgye-Nagy, Á., Szemán-Nagy, A., Sayed-Ahmad, M., & Héjja-Nagy, K. (2023). Effects of health anxiety, social support, and coping on dissociation with mediating role of perceived stress during the COVID-19 pandemic. *International Journal of Environmental Research and Public Health*, *20*(8), 5491. https://doi.org/10.3390/ijerph20085491

Konovalova, I. (2023). *The role of experiential avoidance and effectiveness of a formulation and brief Acceptance and Commitment Therapy intervention for Functional Neurological Disorder* (Doctoral dissertation, University of Southampton). https://doi.org/10.1186/ISRCTN48373551

Koreki, A., Garfkinel, S. N., Mula, M., Agrawal, N., Cope, S., Eilon, T., ... & Yogarajah, M. (2020). Trait and state interoceptive abnormalities are associated with dissociation and seizure frequency in patients with functional seizures. *Epilepsia*, *61*(6), 1156-1165. https://doi.org/10.1111/epi.16532

Korol, S. (2008). Familial and social support as protective factors against the development of dissociative identity disorder. *Journal of Trauma & Dissociation*, *9*(2), 249-267. https://doi.org/10.1080/15299730802048744

Koshiyama, D., Miyakoshi, M., Joshi, Y. B., Molina, J. L., Tanaka-Koshiyama, K., Sprock, J., ... & Light, G. A. (2021). Neural network dynamics underlying gamma synchronization deficits in schizophrenia. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *107*, 110224. https://doi.org/10.1016/j.pnpbp.2020.110224

Kotsiantis, S. B., Zaharakis, I., & Pintelas, P. (2007). Supervised machine learning: A review of classification techniques. *Emerging artificial intelligence applications in computer engineering*, *160*(1), 3-24.

Kovacs, D., Eszlari, N., Petschner, P., Pap, D., Vas, S., Kovacs, P., ... & Bagdy, G. (2016). Effects of IL1B single nucleotide polymorphisms on depressive and anxiety symptoms are determined by severity and type of life stress. *Brain, behavior, and immunity*, *56*, 96-104. https://doi.org/10.1016/j.bbi.2016.02.012

Kowiański, P., Lietzau, G., Czuba, E., Waśkow, M., Steliga, A., & Moryś, J. (2018). BDNF: a key factor with multipotent impact on brain signaling and synaptic plasticity. *Cellular and molecular neurobiology*, *38*, 579-593. https://doi.org/10.1007/s10571-017-0510-4

Kozlowska, K. (2017). A stress-system model for functional neurological symptoms. *Journal of the neurological sciences*, *383*, 151-152. https://doi:10.1016/j.jns.2017.10.044

Kozlowska, K. A. S. I. A., Nunn, K. P., Rose, D., Morris, A. N. N. E., Ouvrier, R. A., & Varghese, J. O. H. N. (2007). Conversion disorder in Australian pediatric practice. *Journal of the American Academy of Child & Adolescent Psychiatry*, *46*(1), 68-75. https://doi.org/10.1097/01.chi.0000242235.83140.1f

Kozlowska, K., Chung, J., Cruickshank, B., McLean, L., Scher, S., Dale, R. C., ... & Patrick, E. (2019). Blood CRP levels are elevated in children and adolescents with functional neurological symptom disorder. *European Child & Adolescent Psychiatry*, *28*, 491-504. https://doi.org/10.1007/s00787-018-1212-2

Kozlowska, K., Palmer, D. M., Brown, K. J., McLean, L., Scher, S., Gevirtz, R., ... & Williams, L. M. (2015). Reduction of autonomic regulation in children and adolescents with

conversion disorders. *Psychosomatic Medicine*, *77*(4), 356-370. https://doi.org/10.1097/PSY.0000000000000184

Kozlowska, K., Schollar-Root, O., Savage, B., Hawkes, C., Chudleigh, C., Raghunandan, J., ... & Helgeland, H. (2023). Illness-Promoting Psychological Processes in Children and Adolescents with Functional Neurological Disorder. *Children*, *10*(11), 1724. https://doi.org/10.3390/children10111724

Kozlowska, K., Spooner, C. J., Palmer, D. M., Harris, A., Korgaonkar, M. S., Scher, S., & Williams, L. M. (2018). "Motoring in idle": The default mode and somatomotor networks are overactive in children and adolescents with functional neurological symptoms. *NeuroImage: Clinical*, *18*, 730-743. https://doi.org/10.1016/j.nicl.2018.02.003

Krafft, A. M., Martin-Krumm, C., & Fenouillet, F. (2019). Adaptation, further elaboration, and validation of a scale to measure hope as perceived by people: Discriminant value and predictive utility vis-à-vis dispositional hope. *Assessment*, *26*(8), 1594-1609. https://doi.org/10.1177/1073191117700724

Kranick, S., Ekanayake, V., Martinez, V., Ameli, R., Hallett, M., & Voon, V. (2011). Psychopathology and psychogenic movement disorders. *Movement Disorders*, *26*(10), 1844-1850. https://doi.org/10.1002/mds.23830

Krause-Utz, A., Frost, R., Winter, D., & Elzinga, B. M. (2017). Dissociation and alterations in brain function and structure: implications for borderline personality disorder. *Current psychiatry reports*, *19*, 1-22. https://doi.org/10.1007/s11920-017-0757-y

Kristensen, T. S., Borritz, M., Villadsen, E., & Christensen, K. B. (2005). The Copenhagen Burnout Inventory: A new tool for the assessment of burnout. *Work & stress*, *19*(3), 192-207. https://doi.org/10.1080/02678370500297720

Kronfol, Z., & Remick, D. G. (2000). Cytokines and the Brain: Implications for Clinical Psychiatry. American Journal of Psychiatry, 157(5), 683–694. https://doi.org/10.1176/appi.ajp.157.5.683

Kuloglu, M., Atmaca, M., Tezcan, E., Gecici, O., & Bulut, S. (2003). Sociodemographic and clinical characteristics of patients with conversion disorder in Eastern Turkey. *Social*

psychiatry and psychiatric epidemiology, *38*, 88-93. https://doi.org/10.1007/s00127-003-0608-5

Kurginyan, S. S., & Osavolyuk, E. Y. (2018). Psychometric Properties of a Russian Version of the Cognitive Flexibility Inventory (CFI-R). *Frontiers in psychology*, *9*, 845. https://doi.org/10.3389/fpsyg.2018.00845

Kushnir, V. A., Solouki, S., Sarig-Meth, T., Vega, M. G., Albertini, D. F., Darmon, S. K., ... & Gleicher, N. (2016). Systemic inflammation and autoimmunity in women with chronic endometritis. *American Journal of Reproductive Immunology*, *75*(6), 672-677. https://doi.org/10.1111/aji.12508

Kutlubaev, M. A., Xu, Y., Hackett, M. L., & Stone, J. (2018). Dual diagnosis of epilepsy and psychogenic nonepileptic seizures: systematic review and meta-analysis of frequency, correlates, and outcomes. *Epilepsy & Behavior*, *89*, 70-78. https://doi.org/10.1016/j.yebeh.2018.10.010

Kwapil, T. R., Wrobel, M. J., & Pope, C. A. (2002). The five-factor personality structure of dissociative experiences. *Personality and individual differences*, *32*(3), 431-443. https://doi.org/10.1016/S0191-8869(01)00035-6

Labate, A., Cerasa, A., Mula, M., Mumoli, L., Gioia, M. C., Aguglia, U., Quattrone, A., & Gambardella, A. (2012). Neuroanatomic correlates of psychogenic nonepileptic seizures: a cortical thickness and VBM study. *Epilepsia*, *53*(2), 377-385. https://doi:10.1111/j.1528-1167.2011.03347.x

LaFrance Jr, W. C., Baker, G. A., Duncan, R., Goldstein, L. H., & Reuber, M. (2013). Minimum requirements for the diagnosis of psychogenic nonepileptic seizures: a staged approach: a report from the International League Against Epilepsy Nonepileptic Seizures Task Force. *Epilepsia*, *54*(11), 2005-2018. https://doi.org/10.1111/epi.12356

LaFrance Jr, W. C., Miller, I. W., Ryan, C. E., Blum, A. S., Solomon, D. A., Kelley, J. E., & Keitner, G. I. (2009). Cognitive behavioral therapy for psychogenic nonepileptic seizures. *Epilepsy & Behavior*, *14*(4), 591-596. https://doi.org/10.1016/j.yebeh.2009.02.016

Lamb, R., Hoston, D., Lin, J., & Firestone, J. (2021). Psychological allostatic load: The cost of persistence in STEM disciplines. *Research in Science Education*, 1-20. https://doi.org/10.1007/s11165-021-10000-2

Lambert, C., Da Silva, S., Ceniti, A. K., Rizvi, S. J., Foussias, G., & Kennedy, S. H. (2018). Anhedonia in depression and schizophrenia: a transdiagnostic challenge. *CNS neuroscience & therapeutics*, *24*(7), 615-623. https://doi.org/10.1111/cns.12854

Lambon Ralph, M. A., Lowe, C., & Rogers, T. T. (2007). Neural basis of category-specific semantic deficits for living things: evidence from semantic dementia, HSVE and a neural network model. *Brain*, *130*(4), 1127-1137. https://doi.org/10.1093/brain/awm025

Lambregts, B. I. H. M., Vassena, E., Jansen, A., Stremmelaar, D. E., Pickkers, P., Kox, M., ... & Van Der Schaaf, M. E. (2023). Fatigue during acute systemic inflammation is associated with reduced mental effort expenditure while task accuracy is preserved. *Brain, Behavior, and Immunity*, *112*, 235-245. https://doi.org/10.1016/j.bbi.2023.05.013

Langeheine, R. (1988). Manifest and latent Markov chain models for categorical panel data. *Journal of Educational Statistics*, *13*(4), 299-312. https://doi.org/10.3102/10769986013004299

Langsted, A., Kamstrup, P. R., & Nordestgaard, B. G. (2014). Lipoprotein (a): fasting and nonfasting levels, inflammation, and cardiovascular risk. *Atherosclerosis*, *234*(1), 95-101. https://doi.org/10.1016/j.atherosclerosis.2014.01.049

Lanius, R. A. (2015). Trauma-related dissociation and altered states of consciousness: a call for clinical, treatment, and neuroscience research. *European Journal of Psychotraumatology*, *6*(1), 27905. https://doi.org/10.3402/ejpt.v6.27905

Lanza, S. T., & Rhoades, B. L. (2013). Latent class analysis: an alternative perspective on subgroup analysis in prevention and treatment. *Prevention science*, *14*(2), 157-168. https://doi.org/10.1007/s11121-011-0201-1

Larner, A. J. (2021). Functional cognitive disorders (FCD): how is metacognition involved?. *Brain sciences*, *11*(8), 1082. https://doi.org/10.3390/brainsci11081082

Lawn, R. B., Murchland, A. R., Kim, Y., Chibnik, L. B., Tworoger, S. S., Rimm, E. B., ... & Kubzansky, L. D. (2022). Trauma, psychological distress and markers of systemic inflammation among US women: A longitudinal study. *Psychoneuroendocrinology*, *145*, 105915. https://doi.org/10.1016/j.psyneuen.2022.105915

Leal, G., Bramham, C. R., & Duarte, C. B. (2017). BDNF and hippocampal synaptic plasticity. *Vitamins and hormones*, *104*, 153-195. https://doi.org/10.1016/bs.vh.2016.10.004

Lebois, L. A., Li, M., Baker, J. T., Wolff, J. D., Wang, D., Lambros, A. M., ... & Kaufman, M. L. (2021). Large-scale functional brain network architecture changes associated with trauma-related dissociation. *American Journal of Psychiatry*, *178*(2), 165-173. https://doi.org/10.1176/appi.ajp.2020.19060647

Lee, S., Allendorfer, J. B., Gaston, T. E., Griffis, J. C., Hernando, K. A., Knowlton, R. C., ... & Ver Hoef, L. W. (2015). White matter diffusion abnormalities in patients with psychogenic non-epileptic seizures. *Brain research*, *1620*, 169-176. http://dx.doi.org/10.1016/j.brainres.2015.04.050

Legrain, V., Van Damme, S., Eccleston, C., Davis, K. D., Seminowicz, D. A., & Crombez, G. (2009). A neurocognitive model of attention to pain: behavioral and neuroimaging evidence. *Pain*, *144*(3), 230-232. https://doi.org/10.1016/j.pain.2009.03.020

Lehn, A., Bullock-Saxton, J., Newcombe, P., Carson, A., & Stone, J. (2019). Survey of the perceptions of health practitioners regarding Functional Neurological Disorders in Australia. *Journal of Clinical Neuroscience*, *67*, 114-123. https://doi.org/10.1016/j.jocn.2019.06.008

Lemieux, L., Salek-Haddadi, A., Josephs, O., Allen, P., Toms, N., Scott, C., ... & Fish, D. R. (2001). Event-related fMRI with simultaneous and continuous EEG: description of the method and initial case report. *Neuroimage*, *14*(3), 780-787. https://doi.org/10.1006/nimg.2001.0853

Levin, S. G., & Godukhin, O. V. (2017). Modulating effect of cytokines on mechanisms of synaptic plasticity in the brain. *Biochemistry (Moscow)*, *82*, 264-274. https://doi.org/10.1134/S000629791703004X

Levin, S. G., Pershina, E. V., Bugaev-Makarovskiy, N. A., Chernomorets, I. Y., Konakov, M. V., & Arkhipov, V. I. (2021). Why do levels of anti-inflammatory cytokines increase during memory acquisition?. *Neuroscience*, *473*, 159-169. https://doi.org/10.1016/j.neuroscience.2021.08.007

Levita, L., Mayberry, E., Mehmood, A., & Reuber, M. (2020). Evaluation of LiNES: a new measure of trauma, negative affect, and relationship insecurity over the life span in persons with FND. *The Journal of neuropsychiatry and clinical neurosciences*, *32*(1), 43-49. https://doi:10.1176/appi.neuropsych.19050121

Li, R., Li, Y., An, D., Gong, Q., Zhou, D., & Chen, H. (2015). Altered regional activity and inter-regional functional connectivity in psychogenic non-epileptic seizures. *Scientific reports*, *5*(1), 11635. https://doi.org/10.1038/srep11635

Lidstone, S. C., MacGillivray, L., & Lang, A. E. (2020). Integrated therapy for functional movement disorders: time for a change. *Movement disorders clinical practice*, *7*(2), 169. https://doi.org/ 10.1002/mdc3.12888

Lidstone, S. C., Nassif, W., Juncos, J., Factor, S. A., & Lang, A. E. (2021). Diagnosing functional neurological disorder: seeing the whole picture. *CNS spectrums*, *26*(6), 593-600. https://doi.org/10.1017/S1092852920001996

Lieberz, J., Shamay-Tsoory, S. G., Saporta, N., Esser, T., Kuskova, E., Stoffel-Wagner, B., ... & Scheele, D. (2021). Loneliness and the social brain: how perceived social isolation impairs human interactions. *Advanced Science*, *8*(21), 2102076. https://doi.org/10.1002/advs.202102076

Lightman, S. L., Birnie, M. T., & Conway-Campbell, B. L. (2020). Dynamics of ACTH and cortisol secretion and implications for disease. *Endocrine reviews*, *41*(3), bnaa002. https://doi.org/10.1210/endrev/bnaa002

Lin, E., & Tsai, S. J. (2020). Gene-environment interactions and role of epigenetics in anxiety disorders. *Anxiety disorders: rethinking and understanding recent discoveries*, 93-102. https://doi.org/10.1007/978-981-32-9705-0_6

Lin, M. R., Hwang, H. F., Chen, C. Y., & Chiu, W. T. (2007). Comparisons of the brief form of the World Health Organization Quality of Life and Short Form-36 for persons with

spinal cord injuries. *American journal of physical medicine & rehabilitation*, *86*(2), 104-113. https://doi.org/10.1097/01.phm.0000247780.64373.0e

Linzer, D. A., & Lewis, J. B. (2011). poLCA: An R package for polytomous variable latent class analysis. *Journal of statistical software*, *42*, 1-29. https://doi.org/10.18637/jss.v042.i10

Livneh, H. (2001). Psychosocial adaptation to chronic illness and disability: A conceptual framework. *Rehabilitation counseling bulletin*, *44*(3), 151-160. https://doi.org/10.1177/003435520104400305

Loewenstein, R. J. (2018). Dissociation debates: Everything you know is wrong. *Dialogues in clinical neuroscience*, *20*(3), 229-242. https://doi.org/10.31887/DCNS.2018.20.3/rloewenstein

Lorenz, E. N. (1963). Deterministic nonperiodic flow. *Journal of atmospheric sciences*, *20*(2), 130-141. https://doi.org/10.1175/1520-0469(1963)020<0130:DNF>2.0.CO;2

Lotfinia, S., Soorgi, Z., Mertens, Y., & Daniels, J. (2020). Structural and functional brain alterations in psychiatric patients with dissociative experiences: a systematic review of magnetic resonance imaging studies. *Journal of Psychiatric Research*, *128*, 5-15. https://doi.org/10.1016/j.jpsychires.2020.05.006

Lovibond, P. F., & Lovibond, S. H. (1995). The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. *Behaviour research and therapy*, *33*(3), 335-343. https://doi:10.1016/0005-7967(94)00075-u

Lubke, G., & Neale, M. (2008). Distinguishing between latent classes and continuous factors with categorical outcomes: Class invariance of parameters of factor mixture models. *Multivariate behavioral research*, *43*(4), 592-620. https://doi.org/10.1080/00273170802490673

Luck, S. J. (2005). Ten simple rules for designing ERP experiments. *Event-related potentials: A methods handbook*, *262083337*.

Luck, S. J. (2006). The operation of attention—millisecond by millisecond—over the first half second. https://doi.org/10.7551/mitpress/3015.003.0017

Luck, S. J. (2014). *An introduction to the event-related potential technique*. MIT Press.

Luck, S. J. (2016). Neurophysiology of selective attention. In *Attention* (pp. 257-295). Psychology Press.

Ludwig, L., Pasman, J. A., Nicholson, T., Aybek, S., David, A. S., Tuck, S., ... & Stone, J. (2018). Stressful life events and maltreatment in conversion (functional neurological) disorder: systematic review and meta-analysis of case-control studies. *The Lancet Psychiatry*, *5*(4), 307-320. https://doi.org/10.1016/S2215-0366(18)30051-8

Lupton, D. (2020). Doing fieldwork in a pandemic: Research ethics and digital methods. *SAGE Research Methods.* https://doi.org/10.4135/9781529761111

Lynch, K. (2010). Carelessness: A hidden doxa of higher education. *Arts & Humanities in Higher Education, 9*(1), 54–67. https://doi.org/10.1177/1474022209350104

Lynn, S. J., Maxwell, R., Merckelbach, H., Lilienfeld, S. O., van Heugten-van der Kloet, D., & Miskovic, V. (2019). Dissociation and its disorders: Competing models, future directions, and a way forward. *Clinical psychology review*, *73*, 101755. https://doi.org/10.1016/j.cpr.2019.101755

Lyssenko, L., Schmahl, C., Bockhacker, L., Vonderlin, R., Bohus, M., & Kleindienst, N. (2018). Dissociation in psychiatric disorders: a meta-analysis of studies using the dissociative experiences scale. *American Journal of Psychiatry*, *175*(1), 37-46. https://doi:10.1176/appi.ajp.2017.17010025

Macarenco, M. M., Opariuc-Dan, C., & Nedelcea, C. (2021). Childhood trauma, dissociation, alexithymia, and anger in people with autoimmune diseases: A mediation model. *Child Abuse & Neglect*, *122*, 105322. https://doi.org/10.1016/j.chiabu.2021.105322

MacDuffie, K. E., Grubbs, L., Best, T., LaRoche, S., Mildon, B., Myers, L., ... & Rommelfanger, K. S. (2021). Stigma and functional neurological disorder: a research agenda targeting the clinical encounter. *CNS spectrums*, *26*(6), 587-592. https://doi.org/10.1017/S1092852920002084

MacLean, P. D. (1990). *The triune brain in evolution: Role in paleocerebral functions*. Springer Science & Business Media.

Madden, M., & Speed, E. (2017). Beware zombies and unicorns: Toward critical patient and public involvement in health research in a neoliberal context. *Frontiers in Sociology, 2*, Article 7. https://doi.org/10.3389/fsoc.2017.00007

Maggio, J., Alluri, P. R., Paredes-Echeverri, S., Larson, A. G., Sojka, P., Price, B. H., Aybek, S., & Perez, D. L. (2020). Briquet syndrome revisited: implications for functional neurological disorder. *Brain Communications*, *2*(2), fcaa156. https://doi.org/10.1093/braincomms/fcaa156

Maier, S. F. (2003). Bi-directional immune–brain communication: Implications for understanding stress, pain, and cognition. *Brain, behavior, and immunity*, *17*(2), 69-85. https://doi.org/10.1016/S0889-1591(03)00032-1

Maines, R. P., & Maines, R. (2001). *The technology of orgasm:" Hysteria," the vibrator, and women's sexual satisfaction* (Vol. 24). JHU Press.

Manera, K. E., Smith, B. J., Owen, K. B., Phongsavan, P., & Lim, M. H. (2022). Psychometric assessment of scales for measuring loneliness and social isolation: an analysis of the household, income and labour dynamics in Australia (HILDA) survey. *Health and quality of life outcomes*, *20*(1), 40. https://doi.org/10.1186/s12955-022-01946-6

Marapin, R. S., van der Stouwe, A. M., de Jong, B. M., Gelauff, J. M., Vergara, V. M., Calhoun, V. D., ... & van der Horn, H. J. (2020). The chronnectome as a model for Charcot's 'dynamic lesion'in functional movement disorders. *NeuroImage: Clinical*, *28*, 102381. https://doi.org/10.1016/j.nicl.2020.102381

Marneros, A. (2009). Mood disorders: epidemiology and natural history. *Psychiatry*, *8*(2), 52-55. https://doi.org/10.1016/j.mppsy.2008.10.022

Marotta, A., Fiorio, M., Fracasso, I., Franchini, C. A., Defazio, G., & Tinazzi, M. (2021). Functional neurological disorders as seen by a cohort of general practitioners in northern Italy: evidence from an online survey. *Frontiers in Neurology*, *12*, 583672. https://doi.org/10.3389/fneur.2021.583672

Marsh, H. W., Lüdtke, O., Muthén, B., Asparouhov, T., Morin, A. J., Trautwein, U., & Nagengast, B. (2010). A new look at the big five factor structure through exploratory structural equation modeling. *Psychological assessment*, *22*(3), 471. https://doi.org/10.1037/a0019227

Marshall, J. C., Halligan, P. W., Fink, G. R., Wade, D. T., & Frackowiak, R. S. (1997). The functional anatomy of a hysterical paralysis. *Cognition*, *64*(1), B1-B8. https://doi.org/10.1016/S0010-0277(97)00020-6

Marsland, A. L., Walsh, C., Lockwood, K., & John-Henderson, N. A. (2017). The effects of acute psychological stress on circulating and stimulated inflammatory markers: a systematic review and meta-analysis. *Brain, behavior, and immunity*, *64*, 208-219. https://doi.org/10.1016/j.bbi.2017.01.011

Martini, R., & Willison, H. (2016). Neuroinflammation in the peripheral nerve: Cause, modulator, or bystander in peripheral neuropathies?. *Glia*, *64*(4), 475-486. https://doi.org/10.1002/glia.22899

Mas-Expósito, L., Amador-Campos, J. A., Gómez-Benito, J., & Lalucat-Jo, L. (2011). The World Health Organization quality of life scale brief version: a validation study in patients with schizophrenia. *Quality of life Research*, *20*, 1079-1089. https://doi.org/10.1007/s11136-011-9847-1

Matin, N., Young, S. S., Williams, B., LaFrance Jr, W. C., King, J. N., Caplan, D., ... & Perez, D. L. (2017). Neuropsychiatric associations with gender, illness duration, work disability, and motor subtype in a US functional neurological disorders clinic population. *The Journal of neuropsychiatry and clinical neurosciences*, *29*(4), 375-382. https://doi.org/10.1176/appi.neuropsych.16110302

Mattfeld, A. T., Whitfield-Gabrieli, S., Biederman, J., Spencer, T., Brown, A., Fried, R., & Gabrieli, J. D. (2016). Dissociation of working memory impairments and attention-deficit/hyperactivity disorder in the brain. *NeuroImage: Clinical*, *10*, 274-282. https://doi:10.1016/j.nicl.2015.12.003

Mattila, A. K., Saarni, S. I., Salminen, J. K., Huhtala, H., Sintonen, H., & Joukamaa, M. (2009). Alexithymia and health-related quality of life in a general population. *Psychosomatics*, *50*(1), 59-68. https://doi.org/10.1176/appi.psy.50.1.59

Mattingly, C. (2010). *The paradox of hope: Journeys through a clinical borderland*. University of California Press.

Maurer, C. W., LaFaver, K., Ameli, R., Toledo, R., & Hallett, M. (2015). A biological measure of stress levels in patients with functional movement disorders. *Parkinsonism & related disorders*, *21*(9), 1072-1075. https://doi.org/10.1016/j.parkreldis.2015.06.017

Maurer, C. W., LaFaver, K., Limachia, G. S., Capitan, G., Ameli, R., Sinclair, S., ... & Horovitz, S. G. (2018). Gray matter differences in patients with functional movement

disorders. Neurology, 91(20), e1870-e1879. https://doi.org/10.1212/WNL.0000000000006514

Maurer, C. W., Liu, V. D., LaFaver, K., Ameli, R., Wu, T., Toledo, R., ... & Hallett, M. (2016). Impaired resting vagal tone in patients with functional movement disorders. *Parkinsonism & related disorders*, *30*, 18-22. https://doi.org/10.1016/j.parkreldis.2016.06.009

McAfoose, J., & Baune, B. T. (2009). Evidence for a cytokine model of cognitive function. *Neuroscience & Biobehavioral Reviews*, *33*(3), 355-366. https://doi.org/10.1016/j.neubiorev.2008.10.005

McEwen, B. S. (2003). Mood disorders and allostatic load. *Biological psychiatry*, *54*(3), 200-207. https://doi.org/10.1016/S0006-3223(03)00177-X

McEwen, B. S. (2019). What is the confusion with cortisol?. *Chronic Stress*, *3*, 2470547019833647. https://doi.org/10.1177/2470547019833647

McEwen, B. S., & Gianaros, P. J. (2011). Stress-and allostasis-induced brain plasticity. *Annual review of medicine*, *62*, 431-445. https://doi.org/10.1146/annurev-med-052209-100430

McEwen, B. S., Gray, J. D., & Nasca, C. (2015). 60 years of neuroendocrinology: redefining neuroendocrinology: stress, sex and cognitive and emotional regulation. *Journal of endocrinology*, *226*(2), T67-T83. https://doi.org/10.1530/JOE-15-0121

McInnes, I. B., & Schett, G. (2017). Pathogenetic insights from the treatment of rheumatoid arthritis. *The Lancet*, *389*(10086), 2328-2337. https://doi.org/10.1016/S0140-6736(17)31472-1

McKenzie, P. S., Oto, M., Graham, C. D., & Duncan, R. (2011). Do patients whose psychogenic non-epileptic seizures resolve,'replace'them with other medically unexplained symptoms? Medically unexplained symptoms arising after a diagnosis of psychogenic non-epileptic seizures. *Journal of Neurology, Neurosurgery & Psychiatry*, *82*(9), 967-969. https://doi.org/10.1136/jnnp.2010.231886

McKim, D. B., Niraula, A., Tarr, A. J., Wohleb, E. S., Sheridan, J. F., & Godbout, J. P. (2016). Neuroinflammatory dynamics underlie memory impairments after repeated social defeat. *Journal of Neuroscience*, *36*(9), 2590-2604. https://doi.org/10.1523/JNEUROSCI.2394-15.2016

McLoughlin, C., Hoeritzauer, I., Cabreira, V., Aybek, S., Adams, C., Alty, J., ... & McWhirter, L. (2023). Functional neurological disorder is a feminist issue. *Journal of Neurology, Neurosurgery & Psychiatry*, *94*(10), 855-862. https://doi.org/10.1136/jnnp-2022-330192

McSweeney, M., Reuber, M., & Levita, L. (2017). Neuroimaging studies in patients with psychogenic non-epileptic seizures: A systematic meta-review. NeuroImage : Clinical, 16, 210-221. https://doi.org/10.1016/j.nicl.2017.07.025

McTeague, L. M., & Lang, P. J. (2012). The anxiety spectrum and the reflex physiology of defense: from circumscribed fear to broad distress. *Depression and anxiety*, *29*(4), 264–281. https://doi.org/10.1002/da.21891

McWhirter, L., Ritchie, C. W., Stone, J., & Carson, A. (2020a). Performance validity test failure in clinical populations—a systematic review. *Journal of Neurology, Neurosurgery & Psychiatry*, *91*(9), 945-952. https://doi.org/10.1136/jnnp-2020-323776

McWhirter, L., Ritchie, C., Stone, J., & Carson, A. (2020). Functional cognitive disorders: a systematic review. *The Lancet Psychiatry*, *7*(2), 191-207. https://doi.org/10.1016/S2215-0366(19)30405-5

McWhirter, L., Ritchie, C., Stone, J., & Carson, A. (2020b). Functional cognitive disorders: a systematic review. *The Lancet Psychiatry*, *7*(2), 191-207. https://doi.org/10.1016/S2215-0366(19)30405-5

McWhirter, L., Stone, J., Sandercock, P., & Whiteley, W. (2011). Hoover's sign for the diagnosis of functional weakness: a prospective unblinded cohort study in patients with suspected stroke. *Journal of psychosomatic research*, *71*(6), 384-386. https://doi:10.1016/j.jpsychores.2011.09.003

Medford, N. (2014). Dissociative symptoms and epilepsy. *Epilepsy & Behavior*, *30*, 10-13. https://doi.org/10.1016/j.yebeh.2013.09.038

Medford, N., Baker, D., Hunter, E., Sierra, M., Lawrence, E., Phillips, M. L., & David, A. S. (2003). Chronic depersonalization following illicit drug use: a controlled analysis of 40 cases. *Addiction*, *98*(12), 1731-1736. https://doi.org/10.1111/j.1360-0443.2003.00548.x

Meltzer, H. (2003). Oslo Social Support Scale-3 [Database record]. Retrieved from PsycTESTS. doi: https://dx.doi.org/10.1037/t75682-000

Meppelink, A. M., Little, S., Oswal, A., Erro, R., Kilner, J., Tijssen, M. A. J., ... & Edwards, M. (2016). Event related desynchronisation predicts functional propriospinal myoclonus. *Parkinsonism & related disorders*, *31*, 116-118. https://doi.org/10.1016/j.parkreldis.2016.07.010

Merone, L., Tsey, K., Russell, D., & Nagle, C. (2022). "I Just Want to Feel Safe Going to a Doctor": Experiences of Female Patients with Chronic Conditions in Australia. *Women's Health Reports*, *3*(1), 1016-1028. https://doi.org/10.1089/whr.2022.0052

Meyers, L. S., Gamst, G., & Guarino, A. J. (2016). *Applied multivariate research: Design and interpretation*. Sage publications.

Miani, A., Pedersen, A. S., Rask, C. U., Uber-Zak, L., Zak, P. J., & Winterdahl, M. (2019). Predicting psychogenic non-epileptic seizures from serum levels of neuropeptide Y and adrenocorticotropic hormone. *Acta Neuropsychiatrica*, *31*(3), 167-171. https://doi.org/10.1017/neu.2019.3

Milano, B. A., Moutoussis, M., & Convertino, L. (2023). The neurobiology of functional neurological disorders characterised by impaired awareness. *Frontiers in Psychiatry*, *14*, 1122865. https://doi.org/10.3389/fpsyt.2023.1122865

Miller, A. H., Maletic, V., & Raison, C. L. (2009). Inflammation and its discontents: the role of cytokines in the pathophysiology of major depression. *Biological psychiatry*, *65*(9), 732-741. https://doi.org/10.1016/j.biopsych.2008.11.029

Milligan, E. D., & Watkins, L. R. (2009). Pathological and protective roles of glia in chronic pain. *Nature reviews neuroscience*, *10*(1), 23-36. https://doi.org/10.1038/nrn2533

Millman, L. M., Short, E., Ward, E., Stanton, B., Bradley-Westguard, A., Goldstein, L. H., ... & Pick, S. (2024). Etiological Factors and Symptom Triggers in Functional Motor Symptoms and Functional Seizures: A Pilot Investigation. *The Journal of Neuropsychiatry and Clinical Neurosciences*, appi-neuropsych. https://doi.org/10.1176/appi.neuropsych.20230103

Minello, A., Martucci, S., & Manzo, L. K. C. (2021). The pandemic and the academic mothers: Present hardships and future perspectives. *European Societies, 23*(1), S82–S94. https://doi.org/10.1080/14616696.2020.1809690

Mittelbronn, M., Dietz, K., Schluesener, H. J., & Meyermann, R. (2001). Local distribution of microglia in the normal adult human central nervous system differs by up to one order of magnitude. *Acta neuropathologica*, *101*, 249-255. https://doi.org/10.1007/s004010000284

Monsa, R., Peer, M., & Arzy, S. (2018). Self-reference, emotion inhibition and somatosensory disturbance: preliminary investigation of network perturbations in conversion disorder. *European journal of neurology*, *25*(6), 888-e62. https://doi.org/10.1111/ene.13613

Montgomery, A. P., Azuero, A., Baernholdt, M., Loan, L. A., Miltner, R. S., Qu, H., ... & Patrician, P. A. (2021). Nurse burnout predicts self-reported medication administration errors in acute care hospitals. *The Journal for Healthcare Quality (JHQ)*, *43*(1), 13-23. https://doi.org/10.1097/JHQ.0000000000000274

Moreau, M. P., & Bernard, C. (2018). Academic motherhood: Exploring barriers and enablers for gender equality in higher education. *Gender and Education, 30*(5), 518–535. https://doi.org/10.1080/09540253.2016.1263937

Moreno-Fernández, M. M., & Matute, H. (2020). Biased Sampling and Causal Estimation of Health-Related Information: Laboratory-Based Experimental Research. *Journal of medical Internet research*, *22*(7), e17502. https://doi.org/10.2196/17502

Morgante, F., Edwards, M. J., Espay, A. J., Fasano, A., Mir, P., Martino, D., & DISMOV-SIN Study Group on Psychogenic Movement Disorders. (2012). Diagnostic agreement in patients with psychogenic movement disorders. *Movement disorders*, *27*(4), 548-552. https://doi.org/10.1002/mds.24903

Morris, L. S., To, B., Baek, K., Chang-Webb, Y. C., Mitchell, S., Strelchuk, D., ... & Voon, V. (2017). Disrupted avoidance learning in functional neurological disorder: implications for harm avoidance theories. *NeuroImage: Clinical*, *16*, 286-294. https://doi.org/10.1016/j.nicl.2017.08.007

Morsy, S. K., Aybek, S., Carson, A., Nicholson, T. R., Stone, J., Kamal, A. M., ... & Kanaan, R. A. (2022). The relationship between types of life events and the onset of functional neurological (conversion) disorder in adults: a systematic review and meta-analysis. *Psychological medicine*, *52*(3), 401-418. https://doi.org/10.1017/S0033291721004669

Mu, J., Chaudhuri, K. R., Bielza, C., de Pedro-Cuesta, J., Larrañaga, P., & Martinez-Martin, P. (2017). Parkinson's disease subtypes identified from cluster analysis of motor and non-motor symptoms. *Frontiers in aging neuroscience*, *9*, 301. https://doi.org/10.3389/fnagi.2017.00301

Muehsam, D., Lutgendorf, S., Mills, P. J., Rickhi, B., Chevalier, G., Bat, N., ... & Gurfein, B. (2017). The embodied mind: a review on functional genomic and neurological correlates of mind-body therapies. *Neuroscience & Biobehavioral Reviews*, *73*, 165-181. https://doi.org/10.1016/j.neubiorev.2016.12.027

Murakami, S., & Okada, Y. (2006). Contributions of principal neocortical neurons to magnetoencephalography and electroencephalography signals. *The Journal of physiology*, *575*(3), 925-936. https://doi.org/10.1113/jphysiol.2006.105379

Myers, L., Trobliger, R., Bortnik, K., Zeng, R., Saal, E., & Lancman, M. (2019). Psychological trauma, somatization, dissociation, and psychiatric comorbidities in patients with psychogenic nonepileptic seizures compared with those in patients with intractable partial epilepsy. *Epilepsy & Behavior*, pp. *92*, 108-113. https://doi:10.1016/j.yebeh.2018.12.027

Myers, R. R., Campana, W. M., & Shubayev, V. I. (2006). The role of neuroinflammation in neuropathic pain: mechanisms and therapeutic targets. *Drug discovery today*, *11*(1-2), 8-20. https://doi.org/10.1016/S1359-6446(05)03637-8

Nagata, K., Tagawa, K., Hiroi, S., Shishido, F., & Uemura, K. (1989). Electroencephalographic correlates of blood flow and oxygen metabolism provided by positron emission tomography in patients with cerebral infarction. *Electroencephalography and clinical neurophysiology*, *72*(1), 16-30. https://doi.org/10.1016/0013-4694(89)90027-8

Nagin, D. (2005). *Group-based modeling of development*. Harvard University Press. https://doi.org/10.4159/9780674041318

Najjar, S., Pearlman, D. M., Alper, K., Najjar, A., & Devinsky, O. (2013). Neuroinflammation and psychiatric illness. *Journal of neuroinflammation*, *10*, 1-24. https://doi.org/10.1186/1742-2094-10-43

Nater, U., Fischer, S., & Ehlert, U. (2011). Stress as a pathophysiological factor in functional somatic syndromes. *Current Psychiatry Reviews*, *7*(2), 152-169. https://doi.org/10.2174/157340011796391184

Nathan, C., & Ding, A. (2010). Nonresolving inflammation. *Cell*, *140*(6), 871-882. https://doi.org/10.1016/j.cell.2010.02.029

Nettleton, S. (2006). 'I just want permission to be ill': towards a sociology of medically unexplained symptoms. *Social science & medicine*, *62*(5), 1167-1178. https://doi.org/10.1016/j.socscimed.2005.07.030

Newbold, D. J., Laumann, T. O., Hoyt, C. R., Hampton, J. M., Montez, D. F., Raut, R. V., ... & Dosenbach, N. U. (2020). Plasticity and spontaneous activity pulses in disused human brain circuits. *Neuron*, *107*(3), 580-589. https://doi.org/10.1016/j.neuron.2020.05.007

Nicholson, T. R., Aybek, S., Kempton, M. J., Daly, E. M., Murphy, D. G., David, A. S., & Kanaan, R. A. (2014). A structural MRI study of motor conversion disorder: evidence of reduction in thalamic volume. *Journal of Neurology, Neurosurgery & Psychiatry*, *85*(2), 227-229. https://doi.org/10.1136/jnnp-2013-305012

Nicholson, T. R., Carson, A., Edwards, M. J., Goldstein, L. H., Hallett, M., Mildon, B., ... & FND-COM (Functional Neurological Disorders Core Outcome Measures) Group. (2020). Outcome measures for functional neurological disorder: a review of the theoretical complexities. *The Journal of neuropsychiatry and clinical neurosciences*, *32*(1), 33-42. https://doi.org/10.1176/appi.neuropsych.19060128

Nicholson, T. R., Stone, J., & Kanaan, R. A. (2011). Conversion disorder: a problematic diagnosis. *Journal of Neurology, Neurosurgery & Psychiatry*, *82*(11), 1267-1273. https://doi.org/10.1136/jnnp.2008.171306

Nicholson, T., Carson, A., Edwards, M., Goldstein, L., Hallett, M., & Mildon, B. et al. (2020). Outcome Measures for Functional Neurological Disorder: A Review of the Theoretical

Complexities. *The Journal Of Neuropsychiatry And Clinical Neurosciences*, *32*(1), 33-42. https://doi:10.1176/appi.neuropsych.19060128

Nijenhuis, E. R., & van der Hart, O. (2011). Dissociation in trauma: A new definition and comparison with previous formulations. *Journal of Trauma & Dissociation*, *12*(4), 416-445. https://doi:10.1080/15299732.2011.570592

Nijenhuis, E. R., Van Der Hart, O., Kruger, K., & Steele, K. (2004). Somatoform dissociation, reported abuse and animal defence-like reactions. *Australian & New Zealand Journal of Psychiatry*, *38*(9), 678-686. https://doi.org/10.1080/j.1440-1614.2004.01441.x

Nijenhuis, E., van der Hart, O., & Steele, K. (2010). Trauma-related structural dissociation of the personality. *Activitas Nervosa Superior*, *52*, 1-23. https://doi.org/10.1007/BF03379560

Nisticò, V., Goeta, D., Iacono, A., Tedesco, R., Giordano, B., Faggioli, R., ... & Demartini, B. (2022). Clinical overlap between functional neurological disorders and autism spectrum disorders: a preliminary study. *Neurological Sciences*, *43*(8), 5067-5073. https://doi.org/10.1007/s10072-022-06048-1

Novakova, B., Harris, P. R., & Reuber, M. (2017). Diurnal patterns and relationships between physiological and self-reported stress in patients with epilepsy and psychogenic non-epileptic seizures. *Epilepsy & Behavior*, *70*, 204-211. https://doi.org/10.1016/j.yebeh.2017.03.006

Nylund, K. L., Asparouhov, T., & Muthén, B. O. (2007). Deciding on the number of classes in latent class analysis and growth mixture modeling: A Monte Carlo simulation study. *Structural equation modeling: A multidisciplinary Journal*, *14*(4), 535-569. https://doi.org/10.1080/10705510701575396

Oathes, D. J., & Ray, W. J. (2008). Dissociative tendencies and facilitated emotional processing. *Emotion*, *8*(5), 653. https://doi.org/10.1037/a0013442

Oldenburg, K. S., O'Shea, T. M., & Fry, R. C. (2020, June). Genetic and epigenetic factors and early life inflammation as predictors of neurodevelopmental outcomes. In *Seminars in Fetal and Neonatal Medicine* (Vol. 25, No. 3, p. 101115). WB Saunders. https://doi.org/10.1016/j.siny.2020.101115

Osipova, E. D., Semyachkina-Glushkovskaya, O. V., Morgun, A. V., Pisareva, N. V., Malinovskaya, N. A., Boitsova, E. B., ... & Salmina, A. B. (2018). Gliotransmitters and cytokines in the control of blood-brain barrier permeability. *Reviews in the Neurosciences*, *29*(5), 567-591. https://doi.org/10.1515/revneuro-2017-0092

Osman, A. H., Alsharief, S. M., & Siddig, H. E. (2020). Functional neurological disorder: characteristics and outcome in a limited-resources country (Sudan). *Epilepsy & Behavior*, *111*, 107151. https://doi.org/10.1016/j.yebeh.2020.107151

Ospina, J. P., Larson, A. G., Jalilianhasanpour, R., Williams, B., Diez, I., Dhand, A., ... & Perez, D. L. (2019). Individual differences in social network size linked to nucleus accumbens and hippocampal volumes in functional neurological disorder: A pilot study. *Journal of affective disorders*, *258*, 50-54. https://doi.org/10.1016/j.jad.2019.07.061

Otten, L. J., & Rugg, M. D. (2005). Interpreting event-related brain potentials. *Event-related potentials: A methods handbook*, 3-16.

Ouss, L., & Tordjman, E. (2014). Conversive disorders among children and adolescents: towards new "complementarist" paradigms?. *Neurophysiologie Clinique/Clinical Neurophysiology*, *44*(4), 411-416. https://doi.org/10.1016/j.neucli.2014.07.004

Özdemir, O., Özdemir, P. G., Boysan, M., & Yilmaz, E. (2015). The relationships between dissociation, attention, and memory dysfunction. *Nöro Psikiyatri Arşivi*, *52*(1), 36. https://doi.org/10.5152/npa.2015.7390

Paredes-Echeverri, S., Guthrie, A. J., & Perez, D. L. (2022). Toward a possible trauma subtype of functional neurological disorder: impact on symptom severity and physical health. *Frontiers in Psychiatry*, *13*, 1040911. https://doi.org/10.3389/fpsyt.2022.1040911

Paredes-Echeverri, S., Maggio, J., Bègue, I., Pick, S., Nicholson, T. R., & Perez, D. L. (2022). Autonomic, endocrine, and inflammation profiles in functional neurological disorder: A systematic review and meta-analysis. *The Journal of neuropsychiatry and clinical neurosciences*, *34*(1), 30-43. https://doi.org/10.1176/appi.neuropsych.21010025

Pareés, I., Kojovic, M., Pires, C., Rubio-Agusti, I., Saifee, T. A., Sadnicka, A., Kassavetis, P., Macerollo A., Bhatia K. P., Carson, A., Stone, J., & Edwards, M. J. (2014). Physical

precipitating factors in functional movement disorders. *Journal of the neurological sciences*, *338*(1-2), 174-177. https://doi:10.1016/j.jns.2013.12.046

Parola, N., Zendjidjian, X. Y., Alessandrini, M., Baumstarck, K., Loundou, A., Fond, G., Berna, F., Lançon, C., Auquier, P., & Boyer, L. (2017). Psychometric properties of the Ruminative Response Scale-short form in a clinical sample of patients with major depressive disorder. *Patient preference and adherence*, *11*, 929–937. https://doi.org/10.2147/PPA.S125730

Pennington, C., Hayre, A., Newson, M., & Coulthard, E. (2015). Functional cognitive disorder: a common cause of subjective cognitive symptoms. *Journal of Alzheimer's Disease*, *48*(s1), S19-S24. https://doi.org/10.3233/JAD-150182

Pepys, M. B., & Hirschfield, G. M. (2003). C-reactive protein: a critical update. *The Journal of clinical investigation*, *111*(12), 1805-1812. https://doi.org/10.1172/JCI200318921

Perez, D. L., & LaFrance, W. C. (2016). Nonepileptic seizures: an updated review. *CNS spectrums*, *21*(3), 239-246. https://doi.org/10.1017/S109285291600002X

Perez, D. L., Aybek, S., Popkirov, S., Kozlowska, K., Stephen, C. D., Anderson, J., ... & American Neuropsychiatric Association Committee for Research. (2021). A review and expert opinion on the neuropsychiatric assessment of motor functional neurological disorders. *The Journal of neuropsychiatry and clinical neurosciences*, *33*(1), 14-26. https://doi.org/10.1176/appi.neuropsych.19120357

Perez, D. L., Matin, N., Barsky, A., Costumero-Ramos, V., Makaretz, S. J., Young, S. S., ... & Dickerson, B. C. (2017). Cingulo-insular structural alterations associated with psychogenic symptoms, childhood abuse and PTSD in functional neurological disorders. *Journal of Neurology, Neurosurgery & Psychiatry*, *88*(6), 491-497. https://doi.org/10.1136/jnnp-2016-314998

Perez, D. L., Matin, N., Williams, B., Tanev, K., Makris, N., LaFrance Jr, W. C., & Dickerson, B. C. (2018). Cortical thickness alterations linked to somatoform and psychological dissociation in functional neurological disorders. *Human brain mapping*, *39*(1), 428-439. https://doi.org/10.1002/hbm.23853

Perez, D. L., Nicholson, T. R., Asadi-Pooya, A. A., Bègue, I., Butler, M., Carson, A. J., ... & Aybek, S. (2021). Neuroimaging in functional neurological disorder: state of the field

and research agenda. *NeuroImage: Clinical*, *30*, 102623. https://doi.org/10.1016/j.nicl.2021.102623

Perez, D. L., Williams, B., Matin, N., LaFrance, W. C., Costumero-Ramos, V., Fricchione, G. L., ... & Dickerson, B. C. (2017). Corticolimbic structural alterations linked to health status and trait anxiety in functional neurological disorder. *Journal of Neurology, Neurosurgery & Psychiatry*, *88*(12), 1052-1059. https://doi.org/10.1136/jnnp-2017-316359

Perjoc, R. S., Roza, E., Vladacenco, O. A., Teleanu, D. M., Neacsu, R., & Teleanu, R. I. (2023). Functional neurological disorder–old problem new perspective. *International Journal of Environmental Research and Public Health*, *20*(2), 1099. https://doi.org/10.3390/ijerph20021099

Perruccio, A. V., Chandran, V., Power, J. D., Kapoor, M., Mahomed, N. N., & Gandhi, R. (2017). Systemic inflammation and painful joint burden in osteoarthritis: a matter of sex?. *Osteoarthritis and cartilage*, *25*(1), 53-59. https://doi.org/10.1016/j.joca.2016.08.001

Petersen, A. M. W., & Pedersen, B. K. (2005). The anti-inflammatory effect of exercise. *Journal of applied physiology*, *98*(4), 1154-1162. https://doi.org/10.1152/japplphysiol.00164.2004

Pettorruso, M., d'Andrea, G., Martinotti, G., Cocciolillo, F., Miuli, A., Di Muzio, I., ... & Camardese, G. (2020). Hopelessness, dissociative symptoms, and suicide risk in major depressive disorder: clinical and biological correlates. *Brain sciences*, *10*(8), 519. https://doi.org/10.3390/brainsci10080519

Pezirkianidis, C., Karakasidou, E., Lakioti, A., Stalikas, A., & Galanakis, M. (2018). Psychometric properties of the depression, anxiety, stress scales-21 (DASS-21) in a Greek sample. *Psychology*, *9*(15), 2933. https://doi.org/10.4236/psych.2018.915170

Pfurtscheller, G., & Aranibar, A. (1977). Event-related cortical desynchronization detected by power measurements of scalp EEG. *Electroencephalography and clinical neurophysiology*, *42*(6), 817-826. https://doi.org/10.1016/0013-4694(77)90235-8

Pick, S., Goldstein, L. H., Perez, D. L., & Nicholson, T. R. (2019). Emotional processing in functional neurological disorder: a review, biopsychosocial model and research

agenda. *Journal of Neurology, Neurosurgery & Psychiatry*, *90*(6), 704-711. https://doi.org/10.1136/jnnp-2018-319201

Pick, S., Mellers, J. D. C., & Goldstein, L. H. (2017). Dissociation in patients with dissociative seizures: relationships with trauma and seizure symptoms. *Psychological medicine*, *47*(7), 1215-1229. https://doi.org/10.1017/S0033291716003093

Pick, S., Mellers, J. D., & Goldstein, L. H. (2016). Emotion and dissociative seizures: a phenomenological analysis of patients' perspectives. *Epilepsy & Behavior*, *56*, 5-14. https://doi.org/10.1016/j.yebeh.2015.12.010

Pick, S., Mellers, J. D., & Goldstein, L. H. (2018). Autonomic and subjective responsivity to emotional images in people with dissociative seizures. *Journal of Neuropsychology*, *12*(2), 341-355. https://doi.org/10.1111/jnp.12144

Pick, S., Millman, L. M., Sun, Y., Short, E., Stanton, B., Winston, J. S., ... & Chalder, T. (2023). Objective and subjective neurocognitive functioning in functional motor symptoms and functional seizures: preliminary findings. *Journal of clinical and experimental neuropsychology*, *45*(10), 970-987. https://doi.org/10.1080/13803395.2023.2245110

Pick, S., Millman, L. M., Ward, E., Short, E., Stanton, B., Reinders, A. S., ... & Mehta, M. A. (2024). Unravelling the influence of affective stimulation on functional neurological symptoms: a pilot experiment examining potential mechanisms. *Journal of Neurology, Neurosurgery & Psychiatry*, *95*(5), 461-470.

Pick, S., Rojas-Aguiluz, M., Butler, M., Mulrenan, H., Nicholson, T. R., & Goldstein, L. H. (2020). Dissociation and interoception in functional neurological disorder. *Cognitive Neuropsychiatry*, *25*(4), 294-311. https://doi.org/10.1080/13546805.2020.1791061

Pierce, M. E., & Albert, D. V. (2022, April). Delivering the Diagnosis: A Practical Approach to a Patient With a Functional Neurological Disorder. In *Seminars in Pediatric Neurology* (Vol. 41, p. 100948). WB Saunders. https://doi.org/10.1016/j.spen.2021.100948

Pike, J. L., & Irwin, M. R. (2006). Dissociation of inflammatory markers and natural killer cell activity in major depressive disorder. *Brain, behavior, and immunity*, *20*(2), 169-174. https://doi.org/10.1016/j.bbi.2005.05.004

Pinquart, M., & Sörensen, S. (2006). Gender differences in caregiver stressors, social resources, and health: An updated meta-analysis. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *61*(1), P33-P45. https://doi.org/10.1093/geronb/61.1.P33

Pollatos, O., Matthias, E., & Keller, J. (2015). When interoception helps to overcome negative feelings caused by social exclusion. *Frontiers in psychology*, *6*, 140662. https://doi.org/10.3389/fpsyg.2015.00786

Pongratz, G., & Straub, R. H. (2014). The sympathetic nervous response in inflammation. *Arthritis research & therapy*, *16*, 1-12. https://doi.org/10.1186/s13075-014-0504-2

Popkirov, S., Hoeritzauer, I., Colvin, L., Carson, A. J., & Stone, J. (2019). Complex regional pain syndrome and functional neurological disorders–time for reconciliation. *Journal of Neurology, Neurosurgery & Psychiatry*, *90*(5), 608-614. https://doi.org/10.1136/jnnp-2018-318298

Popkirov, S., Jungilligens, J., Grönheit, W., & Wellmer, J. (2017). Diagnosing psychogenic nonepileptic seizures: video-EEG monitoring, suggestive seizure induction and diagnostic certainty. *Epilepsy & Behavior*, *73*, 54-58. https://doi.org/10.1016/j.yebeh.2017.05.027

Povoa, P., Coelho, L., Almeida, E., Fernandes, A., Mealha, R., Moreira, P., & Sabino, H. (2005). C-reactive protein as a marker of infection in critically ill patients. *Clinical microbiology and infection*, *11*(2), 101-108. https://doi.org/10.1111/j.1469-0691.2004.01044.x

Power, M., Bullinger, M., & Harper, A. (1999). The World Health Organization WHOQOL-100: tests of the universality of Quality of Life in 15 different cultural groups worldwide. *Health psychology*, *18*(5), 495. https://doi.org/10.1037/0278-6133.18.5.495

Powers, A., Dixon, H. D., Conneely, K., Gluck, R., Munoz, A., Rochat, C., ... & Gillespie, C. F. (2019). The differential effects of PTSD, MDD, and dissociation on CRP in trauma-exposed women. *Comprehensive psychiatry*, *93*, 33-40. https://doi.org/10.1016/j.comppsych.2019.06.007

Powers, A., Dixon, H. D., Conneely, K., Gluck, R., Munoz, A., Rochat, C., ... & Gillespie, C. F. (2019). The differential effects of PTSD, MDD, and dissociation on CRP in trauma-exposed women. *Comprehensive psychiatry*, *93*, 33-40. https://doi.org/10.1016/j.comppsych.2019.06.007

Prasko, J., Ociskova, M., Grambal, A., Sigmundova, Z., Kasalova, P., Marackova, M., ... & Slepecky, M. (2016). Personality features, dissociation, self-stigma, hope, and the complex treatment of depressive disorder. *Neuropsychiatric disease and treatment*, 2539-2552.ystematic review and meta-analysis. *BJPsych open*, *9*(1), e2. https://doi.org/10.2147/NDT.S117037

Prasko, J., Ociskova, M., Sigmundova, Z., Kasalova, P., Grambal, A., Holubova, M., ... & Kotianova, A. (2017). Self-stigma, hope, dissociation, and personality features in treatment of depressive inpatients resistant to pharmacotherapy. *European Psychiatry*, *41*(S1), s244-s244. https://doi.org/10.1016/j.eurpsy.2017.02.019

Price, C. J., & Thompson, E. A. (2007). Measuring dimensions of body connection: body awareness and bodily dissociation. *The Journal of Alternative and Complementary Medicine*, *13*(9), 945-953. https://doi.org/10.1089/acm.2007.0537

Price, J. L., & Drevets, W. C. (2010). Neurocircuitry of mood disorders. *Neuropsychopharmacology*, *35*(1), 192-216. https://doi.org/10.1038/npp.2009.104

Prueter, C., Schultz-Venrath, U., & Rimpau, W. (2002). Dissociative and associated psychopathological symptoms in patients with epilepsy, pseudoseizures, and both seizure forms. *Epilepsia*, *43*(2), 188-192. https://doi.org/10.1046/j.1528-1157.2002.45900.x

Puentes, L. R. (2023). *Functional Neurological Symptom Disorder, Dissociation, and Impairments of Attention: A Psychoneurobiological Perspective* (Doctoral dissertation, Fielding Graduate University).

Purpura, D. P., & McMurtry, J. G. (1965). Intracellular activities and evoked potential changes during polarization of motor cortex. *Journal of neurophysiology*, *28*(1), 166-185. https://doi.org/10.1152/jn.1965.28.1.166

Putman, P., Verkuil, B., Arias-Garcia, E., Pantazi, I., & van Schie, C. (2014). EEG theta/beta ratio as a potential biomarker for attentional control and resilience against deleterious effects of stress on attention. *Cognitive, Affective, & Behavioral Neuroscience*, *14*, 782-791. https://doi.org/10.3758/s13415-013-0238-7

Quinones, M. M., Gallegos, A. M., Lin, F. V., & Heffner, K. (2020). Dysregulation of inflammation, neurobiology, and cognitive function in PTSD: an integrative review. *Cognitive, Affective, & Behavioral Neuroscience*, *20*(3), 455-480. https://doi.org/10.3758/s13415-020-00782-9

Radmanesh, M., Jalili, M., & Kozlowska, K. (2020). Activation of functional brain networks in children with psychogenic non-epileptic seizures. *Frontiers in Human Neuroscience*, *14*, 339. https://doi.org/10.3389/fnhum.2020.00339

Raghavan, S., & Sandanapitchai, P. (2020). The relationship between cultural variables and resilience to psychological trauma: A systematic review of the literature. *Traumatology*.

Rai, S., Foster, S., Griffiths, K. R., Breukelaar, I. A., Kozlowska, K., & Korgaonkar, M. S. (2022). Altered resting-state neural networks in children and adolescents with functional neurological disorder. *NeuroImage: Clinical*, *35*, 103110. https://doi.org/10.1016/j.nicl.2022.103110

Raichle, M. E. (2015). The brain's default mode network. *Annual review of neuroscience*, *38*, 433-447. https://doi.org/10.1146/annurev-neuro-071013-014030

Rajeh, Y. N., Dolatshahi, B., Pourshahbaz, A., & Zarghami, M. (2022). Assessing the validity and reliability of the Dimensional Anhedonia Rating Scale (DARS) for the Iranian population. *Iranian Journal of Psychiatry and Behavioral Sciences*, *16*(2). https://doi.ori/0.5812/ijpbs-120043

Ranford, J., MacLean, J., Alluri, P. R., Comeau, O., Godena, E., LaFrance Jr, W. C., ... & Perez, D. L. (2020). Sensory processing difficulties in functional neurological disorder: a possible predisposing vulnerability?. *Psychosomatics*, *61*(4), 343-352. https://doi.org/10.1016/j.psym.2020.02.003

Ratcliff, J., & van der Feltz-Cornelis, C. (2020). Conversion Disorder/Functional Neurological Disorder–a narrative review on current research into its pathological mechanism. *The*

European Journal of Psychiatry, *34*(3), 143-152. https://doi.org/10.1016/j.ejpsy.2020.03.004

Rather, M. A., & Cavanna, A. E. (2020). Nonepileptic attack disorder and functional movement disorder: A clinical continuum?. *Epilepsy & Behavior*, *106*, 107028. https://doi.org/10.1016/j.yebeh.2020.107028

Raynor, G., & Baslet, G. (2021). A historical review of functional neurological disorder and comparison to contemporary models. *Epilepsy & Behavior Reports*, *16*, 100489. https://doi.org/10.1016/j.ebr.2021.100489

Reuber, M. (2009). The etiology of psychogenic non-epileptic seizures: toward a biopsychosocial model. *Neurologic clinics*, *27*(4), 909-924. https://doi.org/10.1016/j.ncl.2009.06.004

Reuber, M., Blackburn, D. J., Elsey, C., Wakefield, S., Ardern, K. A., Harkness, K., ... & Drew, P. (2018). An interactional profile to assist the differential diagnosis of neurodegenerative and functional memory disorders. *Alzheimer Disease & Associated Disorders*, *32*(3), 197-206. https://doi.org/10.1097/WAD.0000000000000231

Reuber, M., Fernández, G., Bauer, J., Helmstaedter, C., & Elger, C. E. (2002). Diagnostic delay in psychogenic nonepileptic seizures. *Neurology*, *58*(3), 493-495.

Reuber, M., House, A. O., Pukrop, R., Bauer, J., & Elger, C. E. (2003). Somatization, dissociation and general psychopathology in patients with psychogenic non-epileptic seizures. *Epilepsy research*, *57*(2-3), 159-167. https://doi.org/10.1016/j.eplepsyres.2003.11.004

Reuber, M., Howlett, S., Khan, A., & Grünewald, R. A. (2007). Non-epileptic seizures and other functional neurological symptoms: predisposing, precipitating, and perpetuating factors. *Psychosomatics*, *48*(3), 230-238. https://doi.org/10.1176/appi.psy.48.3.230

Revell, E. R., Gillespie, D., Morris, P. G., & Stone, J. (2021). Drop attacks as a subtype of FND: A cognitive behavioural model using grounded theory. *Epilepsy & Behavior Reports*, *16*, 100491. https://doi.org/10.1016/j.ebr.2021.100491

Richter, P., Werner, J., Heerlein, A., Kraus, A., & Sauer, H. (1998). On the validity of the Beck Depression Inventory: A review. *Psychopathology*, *31*(3), 160-168. https://doi.org/10.1159/000066239

Ridker, P. M., Hennekens, C. H., Buring, J. E., & Rifai, N. (2000). C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. *New England journal of medicine*, *342*(12), 836-843. https://doi.org/10.1056/NEJM200003233421202

Rizvi, S. J., Quilty, L. C., Sproule, B. A., Cyriac, A., Bagby, R. M., & Kennedy, S. H. (2015). Development and validation of the Dimensional Anhedonia Rating Scale (DARS) in a community sample and individuals with major depression. *Psychiatry research*, *229*(1-2), 109-119. https://doi.org/10.1016/j.psychres.2015.07.062

Roberts, N. A., Burleson, M. H., Weber, D. J., Larson, A., Sergeant, K., Devine, M. J., ... & Wang, N. C. (2012). Emotion in psychogenic nonepileptic seizures: responses to affective pictures. *Epilepsy & Behavior*, *24*(1), 107-115. https://doi.org/10.1016/j.yebeh.2012.03.018

Ródenas-Perea, G., Velasco-Barbancho, E., Perona-Garcelán, S., Rodríguez-Testal, J. F., Senín-Calderón, C., Crespo-Facorro, B., & Ruiz-Veguilla, M. (2023). Childhood and adolescent trauma and dissociation: the mediating role of rumination, intrusive thoughts and negative affect. *Scandinavian journal of psychology*, *64*(2), 142-149. https://doi.org/10.1111/sjop.12879

Roelofs, K., Keijsers, G. P., Hoogduin, K. A., Näring, G. W., & Moene, F. C. (2002). Childhood abuse in patients with conversion disorder. *American Journal of Psychiatry*, *159*(11), 1908-1913. https://doi.org/10.1176/appi.ajp.159.11.1908

Roelofs, K., Spinhoven, P., Sandijck, P., Moene, F. C., & Hoogduin, K. A. (2005). The impact of early trauma and recent life-events on symptom severity in patients with conversion disorder. *The Journal of nervous and mental disease*, *193*(8), 508-514. https://doi.org/10.1016/j.psyneuen.2005.02.008

Romero-López, M. J. (2016). A review of the dissociative disorders: from multiple personality disorder to the posttraumatic stress. *anales de psicología*, *32*(2), 448. https://doi.org/10.6018/analesps.32.2.218301

Rosemergy, I., Frith, R., Herath, S., & Walker, E. (2013). Use of postictal respiratory pattern to discriminate between convulsive psychogenic nonepileptic seizures and generalized tonic-clonic seizures. *Epilepsy & Behavior*, *27*(1), 81-84. https://doi.org/10.1016/j.yebeh.2012.12.024

Ross, C. A., Joshi, S., & Currie, R. (1990). Dissociative experiences in the general population. *American Journal of Psychiatry*, *147*(11), 1547-1552. https://doi.org/10.1176/ajp.147.11.1547

Rossier, P., & Wade, D. T. (2002). The Guy's Neurological Disability Scale in patients with multiple sclerosis: a clinical evaluation of its reliability and validity. *Clinical Rehabilitation*, *16*(1), 75-95. https://doi.org/10.1191/0269215502cr447oa

Ruiz, F. J., Suárez Falcón, J. C., Sierra, M. A., Barreto Montero, K., García Martín, M. B., Bernal, P. A., & Ramírez, E. S. (2017). Psychometric Properties and Factor Structure of the Ruminative Responses Scale-Short Form in Colombia. International Journal of Psychology and Psychological Therapy, 17(2), 199-208.

Sanchez, P. E., Zhu, L., Verret, L., Vossel, K. A., Orr, A. G., Cirrito, J. R., ... & Mucke, L. (2012). Levetiracetam suppresses neuronal network dysfunction and reverses synaptic and cognitive deficits in an Alzheimer's disease model. *Proceedings of the National Academy of Sciences*, *109*(42), E2895-E2903. https://doi.org/10.1073/pnas.1121081109

Sar, V., & Ozturk, E. (2013). What is trauma and dissociation?. In *Trauma and Dissociation in a Cross-Cultural Perspective* (pp. 7-20). Routledge. https://doi.org/10.1300/J189v04n01_02

Şar, V., Akyüz, G., Kundakçı, T., Kızıltan, E., & Doğan, O. (2004). Childhood trauma, dissociation, and psychiatric comorbidity in patients with conversion disorder. *American Journal of Psychiatry*, *161*(12), 2271-2276. https://doi.org/10.1176/ajp.161.12.2271

Sar, V., Islam, S., & Öztürk, E. (2009). Childhood emotional abuse and dissociation in patients with conversion symptoms. *Psychiatry and clinical neurosciences*, *63*(5), 670-677. https://doi.org/10.1111/j.1440-1819.2009.02012.x

Sashidharan, T., Pawlow, L. A., & Pettibone, J. C. (2012). An examination of racial bias in the Beck Depression Inventory-II. *Cultural diversity & ethnic minority psychology*, *18*(2), 203–209. https://doi.org/10.1037/a0027689

Scott, B. M., Strutt, A. M., & Lundberg-Love, P. (2019). Emotion regulation and neuropsychological status in functional neurological disorder variants. *Rev Iberoam Neuropsicol*, *2*, 30-42.

Schäfer, G., Prkachin, K. M., Kaseweter, K. A., & de C Williams, A. C. (2016). Health care providers' judgments in chronic pain: the influence of gender and trustworthiness. *Pain*, *157*(8), 1618-1625. https://doi.org/10.1097/j.pain.0000000000000536

Schimmenti, A. (2018). The trauma factor: Examining the relationships among different types of trauma, dissociation, and psychopathology. *Journal of Trauma & Dissociation*, *19*(5), 552-571. https://doi.org/10.1080/15299732.2017.1402400

Schlumpf, Y. R., Nijenhuis, E. R., Klein, C., Jäncke, L., & Bachmann, S. (2021). Resting-state functional connectivity in patients with a complex PTSD or complex dissociative disorder before and after inpatient trauma treatment. *Brain and Behavior*, *11*(7), e02200. https://doi.org/10.1002/brb3.2200

Schmalbach, B., Häuser, W., Brähler, E., Henningsen, P., & Wolfe, F. (2021). Fibromyalgia revisited: do latent class analyses of symptom profiles in the general population confirm 2016 fibromyalgia diagnostic criteria?. *Clinical and experimental rheumatology*, *39*(3), S128-S136. https://doi.org/10.55563/clinexprheumatol/bexjsm

Schmidhuber, J. (2015). Deep learning in neural networks: An overview. *Neural networks*, *61*, 85-117. https://doi.org/10.1016/j.neunet.2014.09.003

Schmidt, R., Ruiz, M. H., Kilavik, B. E., Lundqvist, M., Starr, P. A., & Aron, A. R. (2019). Beta oscillations in working memory, executive control of movement and thought, and sensorimotor function. *Journal of Neuroscience*, *39*(42), 8231-8238. https://doi.org/10.1523/JNEUROSCI.1163-19.2019

Schmidt, T., & Vorberg, D. (2006). Criteria for unconscious cognition: Three types of dissociation. *Perception & Psychophysics*, *68*(3), 489-504. https://doi.org/10.3758/BF03193692

Schneider, W., & Chein, J. M. (2003). Controlled & automatic processing: behavior, theory, and biological mechanisms. *Cognitive science*, *27*(3), 525-559. https://doi.org/10.1207/s15516709cog2703_8

Schnorpfeil, P., Noll, A., Schulze, R., Ehlert, U., Frey, K., & Fischer, J. E. (2003). Allostatic load and work conditions. *Social science & medicine*, *57*(4), 647-656. https://doi.org/10.1016/S0277-9536(02)00407-0

Schön, D. A. (1983). *The reflective practitioner: How professionals think in action.* Basic Books.

Schrag, A. E., Mehta, A. R., Bhatia, K. P., Brown, R. J., Frackowiak, R. S., Trimble, M. R., ... & Rowe, J. B. (2013). The functional neuroimaging correlates of psychogenic versus organic dystonia. *Brain*, *136*(3), 770-781. https://doi.org/10.1093/brain/awt008

Schulz, R., & Sherwood, P. R. (2008). Physical and mental health effects of family caregiving. *AJN The American Journal of Nursing*, *108*(9), 23-27. https://doi.org/10.1097/01.NAJ.0000336406.45248.4c

Schurz, M., Uddin, L. Q., Kanske, P., Lamm, C., Sallet, J., Bernhardt, B. C., ... & Bzdok, D. (2021). Variability in brain structure and function reflects lack of peer support. *Cerebral Cortex*, *31*(10), 4612-4627. https://doi.org/10.1093/cercor/bhab109

Seeley, W. W., Menon, V., Schatzberg, A. F., Keller, J., Glover, G. H., Kenna, H., ... & Greicius, M. D. (2007). Dissociable intrinsic connectivity networks for salience processing and executive control. *Journal of neuroscience*, *27*(9), 2349-2356. https://doi.org/10.1523/JNEUROSCI.5587-06.2007

Seignourel, P. J., Miller, K., Kellison, I., Rodriguez, R., Fernandez, H. H., Bauer, R. M., ... & Okun, M. S. (2007). Abnormal affective startle modulation in individuals with psychogenical movement disorder. *Movement disorders: official journal of the Movement Disorder Society*, *22*(9), 1265-1271. https://doi.org/10.1002/mds.21451

Selkirk, M., Duncan, R., Oto, M., & Pelosi, A. (2008). Clinical differences between patients with nonepileptic seizures who report antecedent sexual abuse and those who do not. *Epilepsia*, *49*(8), 1446-1450. https://doi.org/10.1111/j.1528-1167.2008.01611.x

Sereno, M., Quigley, J., & Smith, G. S. (2022). A systematic review of the use of the implicit relational assessment procedure (IRAP) to assess implicit biases held by professionals toward client populations. *Research on Social Work Practice*, *32*(1), 73-91. https://doi.org/10.1177/10497315211009597

Sergerie, K., Lepage, M., & Armony, J. L. (2006). A process-specific functional dissociation of the amygdala in emotional memory. *Journal of Cognitive Neuroscience*, *18*(8), 1359-1367. https://doi.org/10.1162/jocn.2006.18.8.1359

Shackman, A. J., Salomons, T. V., Slagter, H. A., Fox, A. S., Winter, J. J., & Davidson, R. J. (2011). The integration of negative affect, pain and cognitive control in the cingulate cortex. *Nature Reviews Neuroscience*, *12*(3), 154-167 https://doi.org/10.1038/nrn2994

Sharpe, D., & Faye, C. (2006). Non-epileptic seizures and child sexual abuse: a critical review of the literature. *Clinical psychology review*, *26*(8), 1020-1040. https://doi.org/10.1016/j.cpr.2005.11.011

Sharpe, M., & Carson, A. (2001). "Unexplained" somatic symptoms, functional syndromes, and somatization: do we need a paradigm shift?. *Annals of internal medicine*, *134*(9_Part_2), 926-930. https://doi.org/10.7326/0003-4819-134-9_Part_2-200105011-00018

Shaw, A. K., & Ward, L. (2014). Dark thoughts: Why mental health in academia is worse than you think. *Higher Education Research & Development, 33*(5), 901–905. https://doi.org/10.1080/07294360.2014.890575

Sherman, G. D., & Mehta, P. H. (2020). Stress, cortisol, and social hierarchy. *Current opinion in psychology*, *33*, 227-232. https://doi.org/10.1016/j.copsyc.2019.09.013

Sime, D., & Sheridan, M. (2014). Academic parents and work-life balance: Gendered experiences in research institutions. *Studies in Higher Education, 39*(5), 603–620. https://doi.org/10.1080/03075079.2012.724593

Sinanaj, I., Cojan, Y., & Vuilleumier, P. (2015). Inter-individual variability in metacognitive ability for visuomotor performance and underlying brain structures. *Consciousness and Cognition*, *36*, 327-337. https://doi.org/10.1016/j.neuroscience.2015.09.031

Sizer, E., Çobanoğlu, T., & Kaplan, İ. (2023). The role of oxidative stress levels and S100B levels in children with functional neurological disorder: Pediatric functional neurological disorder. *Journal of Surgery and Medicine*, *7*(12), 748-753. https://doi.org/10.28982/josam.7856

Slater, R., Holowka, D., Schorr, Y., & Roemer, L. (2005). Rumination, dissociation, self-compassion, and acceptance as correlates of posttraumatic stress symptoms. *Associat Behav & Cognitive Therapy2005*.

Sleiman, S. F., Henry, J., Al-Haddad, R., El Hayek, L., Abou Haidar, E., Stringer, T., ... & Chao, M. V. (2016). Exercise promotes the expression of brain derived neurotrophic factor (BDNF) through the action of the ketone body β-hydroxybutyrate. *elife*, *5*, e15092. https://doi.org/10.7554/eLife.15092.012

Smith, B. W., Dalen, J., Wiggins, K., Tooley, E., Christopher, P., & Bernard, J. (2008). The brief resilience scale: assessing the ability to bounce back. International journal of behavioral medicine, 15(3), 194-200. https://doi.org/10.1080/10705500802222972

Soffer-Dudek, N. (2014). Dissociation and dissociative mechanisms in panic disorder, obsessive–compulsive disorder, and depression: A review and heuristic framework. *Psychology of Consciousness: Theory, Research, and Practice*, *1*(3), 243. https://doi.org/10.1037/cns0000023

Sojka, P., Bareš, M., Kašpárek, T., & Světlák, M. (2018). Processing of emotion in functional neurological disorder. *Frontiers in psychiatry*, *9*, 479. https://doi.org/10.3389/fpsyt.2018.00479

Sojka, P., Lošák, J., & Lamoš, M. (2019). Processing of emotions in functional movement disorder: An exploratory fMRI study. *Frontiers in Neurology*, *10*, 466657. https://doi.org/10.3389/fneur.2019.00861

Sojka, P., Serranova, T., Khalsa, S., Perez, D., & Diez, I. (2024). Interoceptive disruption in functional neurological disorder: a multimodal brain imaging study. *medRxiv*, 2024-03. https://doi.org/10.1101/2024.03.13.24303546

Sone, D. (2023). White matter structural connectivity and its impact on psychogenic non-epileptic seizures: An evidence-based review. *Neuropsychiatric Disease and Treatment*, 1573-1579. https://doi.org/10.2147/NDT.S402378

Spagnolo, P. A., Norato, G., Maurer, C. W., Goldman, D., Hodgkinson, C., Horovitz, S., & Hallett, M. (2020). Effects of TPH2 gene variation and childhood trauma on the clinical and circuit-level phenotype of functional movement disorders. *Journal of Neurology,*

Neurosurgery & Psychiatry, *91*(8), 814-821. https://doi.org/10.1136/jnnp-2019-322636

Spence, S. A., Crimlisk, H. L., Cope, H., Ron, M. A., & Grasby, P. M. (2000). Discrete neurophysiological correlates in prefrontal cortex during hysterical and feigned disorder of movement. *The Lancet*, *355*(9211), 1243-1244. https://doi.org/10.1016/S0140-6736(00)02096-1

Spiegel, D., & Simeon, D. (2015). Dissociative disorders. *Study Guide to DSM-5*, 195-210.

Spinhoven, P., Roelofs, K., Moene, F., Kuyk, J., Nijenhuis, E., Hoogduin, K., & Van Dyck, R. (2004). Trauma and dissociation in conversion disorder and chronic pelvic pain. *The International Journal of Psychiatry in Medicine*, *34*(4), 305-318. https://doi.org/10.2190/YDK2-C66W-CL6L-N5TK

Spitzer, C., Barnow, S., Freyberger, H. J., & Joergen Grabe, H. (2007). Dissociation predicts symptom-related treatment outcome in short-term inpatient psychotherapy. *Australian & New Zealand Journal of Psychiatry*, *41*(8), 682-687. https://doi.org/10.1080/00048670701449146

Staab, J. P., Eckhardt-Henn, A., Horii, A., Jacob, R., Strupp, M., Brandt, T., & Bronstein, A. (2017). Diagnostic criteria for persistent postural-perceptual dizziness (PPPD): Consensus document of the committee for the Classification of Vestibular Disorders of the Bárány Society. *Journal of Vestibular Research*, *27*(4), 191-208. https://doi.org/10.3233/VES-170622

Staniloiu, A., Borsutzky, S., & Markowitsch, H. J. (2010). Dissociative memory disorders and immigration. In *ASCS09: Proceedings of the 9th Conference of the Australasian Society for Cognitive Science* (pp. 316-324). Centre for Cognitive Science Sydney. https://doi.org/10.5096/ASCS200948

Starck, T., Nikkinen, J., Rahko, J., Remes, J., Hurtig, T., Haapsamo, H., ... & Kiviniemi, V. J. (2013). Resting state fMRI reveals a default mode dissociation between retrosplenial and medial prefrontal subnetworks in ASD despite motion scrubbing. *Frontiers in human neuroscience*, *7*, 802. https://doi.org/10.3389/fnhum.2013.00802

Staton, A., Dawson, D., Merdian, H., Tickle, A., & Walker, T. (2024). Functional neurological disorder: A qualitative study exploring individuals' experiences of psychological

services. *Psychology and Psychotherapy: Theory, Research and Practice*, *97*(1), 138-156. https://doi.org/10.1111/papt.12504

Steer, R. A., Rissmiller, D. J., & Beck, A. T. (2000). Use of the Beck Depression Inventory-II with depressed geriatric inpatients. *Behaviour research and therapy*, *38*(3), 311-318. https://doi.org/10.1016/S0005-7967(99)00068-6

Steffen, A., Fiess, J., Schmidt, R., & Rockstroh, B. (2015). "That pulled the rug out from under my feet!"–adverse experiences and altered emotion processing in patients with functional neurological symptoms compared to healthy comparison subjects. *BMC psychiatry*, *15*, 1-9. https://doi.org/10.1186/s12888-015-0514-x

Stephen, C. D., Perez, D. L., Chibnik, L. B., & Sharma, N. (2021). Functional dystonia: A case-control study and risk prediction algorithm. *Annals of Clinical and Translational Neurology*, *8*(4), 732-748. https://doi.org/10.1002/acn3.51307

Stephenson, C. P., & Baguley, I. J. (2018). Functional neurological symptom disorder (conversion disorder): A role for microglial-based plasticity mechanisms?. *Medical Hypotheses*, *111*, 41-48. https://doi.org/10.1016/j.mehy.2017.12.010

Sterling, P. (1988). Allostasis: a new paradigm to explain arousal pathology. *Handbook of life stress, cognition and health*.

Stevenson, A. J., McCartney, D. L., Hillary, R. F., Campbell, A., Morris, S. W., Bermingham, M. L., ... & Marioni, R. E. (2020). Characterisation of an inflammation-related epigenetic score and its association with cognitive ability. *Clinical Epigenetics*, *12*, 1-11. https://doi.org/10.1186/s13148-020-00903-8

Stewart, K. E., Ross, D., & Hartley, S. (2004). Patient adaptation to chronic illness. https://doi.org/10.1037/11589-013

Stoltenborgh, M., Van Ijzendoorn, M. H., Euser, E. M., & Bakermans-Kranenburg, M. J. (2011). A global perspective on child sexual abuse: Meta-analysis of prevalence around the world. *Child maltreatment*, *16*(2), 79-101. https://doi.org/10.1177/1077559511403920

Stone, J. V. (2004). Independent component analysis: a tutorial introduction. https://doi.org/10.7551/mitpress/3717.001.0001

Stone, J., Binzer, M., & Sharpe, M. (2004). Illness beliefs and locus of control: a comparison of patients with pseudoseizures and epilepsy. *Journal of psychosomatic research*, *57*(6), 541-547. https://doi.org/10.1016/j.jpsychores.2004.03.013

Stone, J., Burton, C., & Carson, A. (2020). Recognising and explaining functional neurological disorder. *bmj*, *371*. https://doi.org/10.1136/bmj.m3745

Stone, J., Campbell, K., Sharma, N., Carson, A. J., Warlow, C. P., & Sharpe, M. (2003). What should we call pseudoseizures? The patient's perspective. Seizure, 12(8), 568- 572. https://doi.org/10.1016/S1059-1311(03)00055-4

Stone, J., Carson, A., Aditya, H., Prescott, R., Zaubi, M., Warlow, C., & Sharpe, M. (2009). The role of physical injury in motor and sensory conversion symptoms: a systematic and narrative review. *Journal of psychosomatic research*, *66*(5), 383-390. https://doi.org/10.1016/j.jpsychores.2008.07.010

Stone, J., Carson, A., Duncan, R., Roberts, R., Warlow, C., Hibberd, C., ... & Sharpe, M. (2010). Who is referred to neurology clinics?—the diagnoses made in 3781 new patients. *Clinical neurology and neurosurgery*, *112*(9), 747-751. https://doi.org/10.1016/j.clineuro.2010.05.011

Stone, J., Pal, S., Blackburn, D., Reuber, M., Thekkumpurath, P., & Carson, A. (2015). Functional (psychogenic) cognitive disorders: a perspective from the neurology clinic. *Journal of Alzheimer's Disease*, *48*(s1), S5-S17. https://doi.org/10.3233/JAD-150430

Stone, J., Sharpe, M., & Binzer, M. (2004). Motor conversion symptoms and pseudoseizures: a comparison of clinical characteristics. *Psychosomatics*, *45*(6), 492-499. https://doi.org/10.1176/appi.psy.45.6.492

Stone, J., Warlow, C., & Sharpe, M. (2010). The symptom of functional weakness: a controlled study of 107 patients. *Brain*, *133*(5), 1537-1551. https://doi.org/10.1093/brain/awq068

Strogatz, S. H. (2018). *Nonlinear dynamics and chaos: with applications to physics, biology, chemistry, and engineering*. CRC press. https://doi.org/10.1201/9780429399640

Su, Q., Yao, D., Jiang, M., Liu, F., Jiang, J., Xu, C., ... & Guo, W. (2014). Dissociation of regional activity in default mode network in medication-naive, first-episode

somatization disorder. *PLoS One*, *9*(7), e99273. https://doi.org/10.1371/journal.pone.0099273

Sullivan, P. F., & Kendler, K. S. (1998). Typology of common psychiatric syndromes: An empirical study. *The British Journal of Psychiatry*, *173*(4), 312-319. https://doi.org/10.1192/bjp.173.4.312

Sullivan, P. F., Smith, W., & Buchwald, D. (2002). Latent class analysis of symptoms associated with chronic fatigue syndrome and fibromyalgia. *Psychological medicine*, *32*(5), 881-888. https://doi.org/10.1017/S0033291702005834

Sumich, A., Anderson, J. D., Howard, C. J., Heym, N., Castro, A., Baker, J., & Belmonte, M. K. (2018). Reduction in lower-alpha power during Ganzfeld flicker stimulation is associated with the production of imagery and trait positive schizotypy. *Neuropsychologia*, *121*, 79-87. https://doi.org/10.1016/j.neuropsychologia.2018.11.004

Sumich, A., Kumari, V., Gordon, E., Tunstall, N., & Brammer, M. (2008). Event-related potential correlates of paranormal ideation and unusual experiences. *Cortex*, *44*(10), 1342-1352. https://doi.org/10.1016/j.cortex.2007.10.012

Suvarna, B., Suvarna, A., Phillips, R., Juster, R. P., McDermott, B., & Sarnyai, Z. (2020). Health risk behaviours and allostatic load: a systematic review. *Neuroscience & Biobehavioral Reviews*, *108*, 694-711. https://doi.org/10.1016/j.neubiorev.2019.12.020

Švob Štrac, D., Pivac, N., & Mück-Šeler, D. (2016). The serotonergic system and cognitive function. *Translational neuroscience*, *7*(1), 35-49. https://doi.org/10.1515/tnsci-2016-0007

Szaflarski, J. P., & LaFrance Jr, W. C. (2018). Psychogenic nonepileptic seizures (PNES) as a network disorder–evidence from neuroimaging of functional (psychogenic) neurological disorders. *Epilepsy currents*, *18*(4), 211-216. https://doi.org/10.5698/1535-7597.18.4.211

Tabachnick, B. G., Fidell, L. S., & Ullman, J. B. (2007). *Using multivariate statistics* (Vol. 5, pp. 481-498). Boston, MA: Pearson.

Tak, L. M., Bakker, S. J., Slaets, J. P., & Rosmalen, J. G. (2009). Is high-sensitive C-reactive protein a biomarker for functional somatic symptoms? A population-based study. *Brain, behavior, and immunity*, *23*(7), 1014-1019. https://doi.org/10.1016/j.bbi.2009.05.059

Teodoro, T., Edwards, M. J., & Isaacs, J. D. (2018). A unifying theory for cognitive abnormalities in functional neurological disorders, fibromyalgia and chronic fatigue syndrome: systematic review. *Journal of Neurology, Neurosurgery & Psychiatry*, *89*(12), 1308-1319. https://doi.org/10.1136/jnnp-2017-317823

Theoharides, T. C., Stewart, J. M., Panagiotidou, S., & Melamed, I. (2016). Mast cells, brain inflammation and autism. *European journal of pharmacology*, *778*, 96-102. https://doi.org/10.1016/j.ejphar.2015.03.086

Thompson-Hollands, J., Jun, J. J., & Sloan, D. M. (2017). The association between peritraumatic dissociation and PTSD symptoms: The mediating role of negative beliefs about the self. *Journal of Traumatic Stress*, *30*(2), 190-194. https://doi.org/10.1002/jts.22179

Thomsen, B. L. C., Teodoro, T., & Edwards, M. J. (2020). Biomarkers in functional movement disorders: a systematic review. *Journal of Neurology, Neurosurgery & Psychiatry*, *91*(12), 1261-1269. https://doi.org/10.1136/jnnp-2020-323141

Thomson, P. (2022). Dissociation and resilience. In *Dissociation and the Dissociative Disorders* (pp. 93-97). Routledge. Chicago.

Tinazzi, M., Fiorio, M., Berardelli, A., Bonetti, B., Bonifati, D. M., Burlina, A., ... & Marotta, A. (2022). Opinion, knowledge, and clinical experience with functional neurological disorders among Italian neurologists: results from an online survey. *Journal of neurology*, 1-11. https://doi.org/10.1007/s00415-021-10840-y

Tinazzi, M., Geroin, C., Erro, R., Marcuzzo, E., Cuoco, S., Ceravolo, R., ... & Morgante, F. (2021). Functional motor disorders associated with other neurological diseases: beyond the boundaries of "organic" neurology. *European journal of neurology*, *28*(5), 1752-1758. https://doi.org/10.1111/ene.14674

Titchkosky, T. (2011). *The question of access: Disability, space, meaning*. University of Toronto Press.

Tiyekli, U., Çalıyurt, O., & Tiyekli, N. D. (2013). Proinflammatory cytokine levels in patients with conversion disorder. *Acta Neuropsychiatrica*, *25*(3), 137-143. https://doi.org/10.1111/j.1601-5215.2012.00676.x

Tojek, T. M., Lumley, M., Barkley, G., Mahr, G., & Thomas, A. (2000). Stress and other psychosocial characteristics of patients with psychogenic nonepileptic seizures. *Psychosomatics*, *41*(3), 221-226. https://doi.org/10.1176/appi.psy.41.3.221

Tolmunen, T., Maaranen, P., Hintikka, J., Kylmä, J., Rissanen, M. L., Honkalampi, K., ... & Laukkanen, E. (2007). Dissociation in a general population of Finnish adolescents. *The Journal of Nervous and Mental Disease*, *195*(7), 614-617. https://doi.org/0.1097/NMD.0b013e318093f487

Toro, M. G., Ruiz, J. S., Talavera, J. A., & Blanco, C. (1999). Chaos theories and therapeutic commonalities among depression, Parkinson's disease, and cardiac arrhythmias. *Comprehensive psychiatry*, *40*(3), 238-244. https://doi.org/10.1016/S0010-440X(99)90011-1

Townshend, K., Hajhashemi, K. (2023). Ruminative Response Scale (RRS). In: Medvedev, O.N., Krägeloh, C.U., Siegert, R.J., Singh, N.N. (eds) Handbook of Assessment in Mindfulness Research. Springer, Cham. https://doi.org/10.1007/978-3-030-77644-2_84-1

Treynor, W., Gonzalez, R., & Nolen-Hoeksema, S. (2003). Rumination reconsidered: A psychometric analysis. Cognitive therapy and research, 27(3), 247-259. https://doi.org/10.1023/A:1023910315561

Tripepi, G., Jager, K. J., Dekker, F. W., & Zoccali, C. (2010). Selection bias and information bias in clinical research. *Nephron Clinical Practice*, *115*(2), c94-c99. https://doi.org/10.1159/000312871

Tureson, K., Gold, A. I., & Thames, A. D. (2022). Inclusion and diversity. In S. M. McClintock & J. Choi (Eds.), *Neuropsychology of depression* (pp. 220–248). The Guilford Press.

Umesh, S., Tikka, S. K., Goyal, N., Sinha, V. K., & Nizamie, S. H. (2017). Aberrant gamma band cortical sources and functional connectivity in adolescents with psychogenic non-epileptic seizures: a preliminary report. *Psychiatry Research*, *247*, 51-54. https://doi.org/10.1016/j.psychres.2016.11.003

Urbanek, M., Harvey, M., McGowan, J., & Agrawal, N. (2014). Regulation of emotions in psychogenic nonepileptic seizures. *Epilepsy & Behavior*, *37*, 110-115. https://doi.org/10.1016/j.yebeh.2014.06.004

van Beilen, M., de Jong, B. M., Gieteling, E. W., Renken, R., & Leenders, K. L. (2011). Abnormal parietal function in conversion paresis. *PLoS One*, *6*(10), e25918. https://doi.org/10.1371/journal.pone.0025918

Van den Bergh, O., Witthöft, M., Petersen, S., & Brown, R. J. (2017). Symptoms and the body: taking the inferential leap. *Neuroscience & Biobehavioral Reviews*, *74*, 185-203. https://doi.org/10.1016/j.neubiorev.2017.01.015

van der Feltz-Cornelis, C., Brabyn, S., Ratcliff, J., Varley, D., Allgar, V., Gilbody, S., Clarke, C., & Lagos, D. (2021). Assessment of cytokines, microRNA and patient related outcome measures in conversion disorder/functional neurological disorder (CD/FND): The CANDO clinical feasibility study. *Brain, behavior, & immunity-health*, *13*, 100228. https://doi.org/10.1016/j.bbih.2021.100228

van der Hoeven, R. M., Broersma, M., Pijnenborg, G. H., Koops, E. A., van Laar, T., Stone, J., & van Beilen, M. (2015). Functional (psychogenic) movement disorders associated with normal scores in psychological questionnaires: a case control study. *Journal of psychosomatic research*, *79*(3), 190-194. https://doi.org/10.1016/j.jpsychores.2015.06.002

van der Kruijs, S. J., Bodde, N. M., Vaessen, M. J., Lazeron, R. H., Vonck, K., Boon, P., ... & Jansen, J. F. (2012). Functional connectivity of dissociation in patients with psychogenic non-epileptic seizures. *Journal of Neurology, Neurosurgery & Psychiatry*, *83*(3), 239-247. https://doi.org/10.1136/jnnp-2011-300776

van der Kruijs, S. J., Jagannathan, S. R., Bodde, N. M., Besseling, R. M., Lazeron, R. H., Vonck, K. E., ... & Jansen, J. F. (2014). Resting-state networks and dissociation in psychogenic non-epileptic seizures. *Journal of psychiatric research*, *54*, 126-133. https://doi.org/10.1016/j.jpsychires.2014.03.010

van der Salm, S. M., Tijssen, M. A., Koelman, J. H., & van Rootselaar, A. F. (2012). The bereitschaftspotential in jerky movement disorders. *Journal of Neurology, Neurosurgery & Psychiatry*, *83*(12), 1162-1167. https://doi.org/10.1136/jnnp-2012-303081

van Dijl, T. L., Aben, H. P., Synhaeve, N. E., de Waardt, D. A., Videler, A. C., & Kop, W. J. (2024). Alexithymia and facial emotion recognition in patients with functional neurological disorder. *Clinical neurology and neurosurgery*, *237*, 108128. https://doi.org/10.1016/j.clineuro.2024.108128

Van Dyken, P., & Lacoste, B. (2018). Impact of Metabolic Syndrome on Neuroinflammation and the Blood–Brain Barrier. *Frontiers in Neuroscience*, *12*, 423804. https://doi.org/10.3389/fnins.2018.00930

Van Lunzen, J., & Altfeld, M. (2014). Sex differences in infectious diseases–common but neglected. *The Journal of infectious diseases*, *209*(suppl_3), S79-S80. https://doi.org/10.1093/infdis/jiu159

van Rooijen, D. E., Geraedts, E. J., Marinus, J., Jankovic, J., & van Hilten, J. J. (2011). Peripheral trauma and movement disorders: a systematic review of reported cases. *Journal of Neurology, Neurosurgery & Psychiatry*, *82*(8), 892-898. https://doi.org/10.1136/jnnp.2010.232504

Vance, R., Clarke, S., O'Keeffe, F., Galligan, T., Doherty, A., Flynn, C., ... & Gillan, D. (2024). Attitudes and perceptions of Irish health care professionals regarding functional neurological disorder: A national survey. *Brain and Behavior*, *14*(2), e3362. https://doi.org/10.1002/brb3.3362

Vanini, G., Bühler, J., Weber, S., Steinauer, M., & Aybek, S. (2024). Healthcare employment as a risk factor for functional neurological disorder: A case–control study. *European journal of neurology*, *31*(1), e16056. https://doi.org/10.1111/ene.16056

Vannikov-Lugassi, M., & Soffer-Dudek, N. (2018). Rumination and dissociation: The mediating role of poor sleep quality and presleep cognitions. *Psychology of Consciousness: Theory, Research, and Practice*, *5*(2), 185. https://doi.org/10.1037/cns0000128

Vargas, J., Spiotta, A., & Chatterjee, A. R. (2019). Initial experiences with artificial neural networks in the detection of computed tomography perfusion deficits. *World neurosurgery*, *124*, e10-e16. https://doi.org/10.1016/j.wneu.2018.10.084

Vassilopoulos, A., Mohammad, S., Dure, L., Kozlowska, K., & Fobian, A. D. (2022). Treatment approaches for functional neurological disorders in children. *Current*

Treatment Options in Neurology, *24*(2), 77-97. https://doi.org/10.1007/s11940-022-00708-5

Vasta, R., Cerasa, A., Sarica, A., Bartolini, E., Martino, I., Mari, F., Metitieri, T., Quattrone, A., Gambardella, A., Guerrini, R., & Labate, A. (2018). The application of artificial intelligence to understand the pathophysiological basis of psychogenic nonepileptic seizures. *Epilepsy & Behavior*, *87*, 167-172. https://doi.org/10.1016/j.yebeh.2018.09.008

Věchetová, G., Slovák, M., Kemlink, D., Hanzlíková, Z., Dušek, P., Nikolai, T., ... & Serranová, T. (2018). The impact of non-motor symptoms on the health-related quality of life in patients with functional movement disorders. *Journal of psychosomatic research*, *115*, 32-37. https://doi.org/10.1016/j.jpsychores.2018.10.001

Verhaeghe, P. (2013). *Does the woman exist?: from Freud's hysteric to Lacan's feminine*. Other Press, Llc.

Villagrán, A., Eldøen, G., Duncan, R., Aaberg, K. M., Hofoss, D., & Lossius, M. I. (2021). Incidence and prevalence of psychogenic nonepileptic seizures in a Norwegian county: a 10-year population-based study. *Epilepsia*, *62*(7), 1528-1535. https://doi.org/10.1111/epi.16949

Vinckier, F., Gourion, D., & Mouchabac, S. J. E. P. (2017). Anhedonia predicts poor psychosocial functioning: results from a large cohort of patients treated for major depressive disorder by general practitioners. *European Psychiatry*, *44*, 1-8. https://doi.org/10.1016/j.eurpsy.2017.02.485

Vogelzangs, N., Beekman, A. T. F., De Jonge, P., & Penninx, B. W. J. H. (2013). Anxiety disorders and inflammation in a large adult cohort. *Translational psychiatry*, *3*(4), e249-e249. https://doi.org/10.1038/tp.2013.27

von Bernhardi, R., Eugenín-von Bernhardi, J., Flores, B., & Eugenín León, J. (2016). Glial cells and integrity of the nervous system. *Glial Cells in Health and Disease of the CNS*, 1-24. https://doi.org/10.1007/978-3-319-40764-7_1

von Bernhardi, R., Eugenín-von Bernhardi, J., Flores, B., & Eugenín León, J. (2016). Glial cells and integrity of the nervous system. *Glial Cells in Health and Disease of the CNS*, 1-24. https://doi.org/10.1007/978-3-319-40764-7_1

Von Korff, M., Alonso, J., Ormel, J., Angermeyer, M., Bruffaerts, R., Fleiz, C., ... & Uda, H. (2009). Childhood psychosocial stressors and adult onset arthritis: broad spectrum risk factors and allostatic load. *Pain*, *143*(1), 76-83. https://doi.org/10.1016/j.pain.2009.01.034

Voon, V., Brezing, C., Gallea, C., & Hallett, M. (2011). Aberrant supplementary motor complex and limbic activity during motor preparation in motor conversion disorder. *Movement Disorders*, *26*(13), 2396-2403. https://doi.org/10.1002/mds.23890

Voon, V., Brezing, C., Gallea, C., Ameli, R., Roelofs, K., LaFrance Jr, W. C., & Hallett, M. (2010). Emotional stimuli and motor conversion disorder. *Brain*, *133*(5), 1526-1536. https://doi.org/10.1093/brain/awq054

Voon, V., Cavanna, A. E., Coburn, K., Sampson, S., Reeve, A., LaFrance Jr, W. C., & American Neuropsychiatric Association Committee for Research). (2016). Functional neuroanatomy and neurophysiology of functional neurological disorders (conversion disorder). *The Journal of neuropsychiatry and clinical neurosciences*, *28*(3), 168-190. https://doi.org/10.1176/appi.neuropsych.14090217

Vuilleumier, P. (2014). Brain circuits implicated in psychogenic paralysis in conversion disorders and hypnosis. *Neurophysiologie Clinique/Clinical Neurophysiology*, *44*(4), 323-337. https://doi.org/10.1016/j.neucli.2014.01.003

Walusinski, O. (2014). The girls of La Salpetriere. *Hysteria: The Rise of an Enigma*, *35*, 65-77. https://doi.org/10.1159/000359993

Walzl, D., Carson, A. J., & Stone, J. (2019). The misdiagnosis of functional disorders as other neurological conditions. *Journal of neurology*, *266*, 2018-2026. https://doi.org/10.1007/s00415-019-09356-3

Wall, S. (2006). An autoethnography on learning about autoethnography. *International journal of qualitative methods*, *5*(2), 146-160. https://doi.org/10.1177/160940690600500205

Waller, N., Putnam, F. W., & Carlson, E. B. (1996). Types of dissociation and dissociative types: A taxometric analysis of dissociative experiences. *Psychological methods*, *1*(3), 300. https://doi.org/10.1037/1082-989X.1.3.300

Wang, H., Zeng, L. L., Chen, Y., Yin, H., Tan, Q., & Hu, D. (2015). Evidence of a dissociation pattern in default mode subnetwork functional connectivity in schizophrenia. *Scientific reports*, *5*(1), 14655. https://doi.org/10.1038/srep14655

Wang, X., Öngür, D., Auerbach, R. P., & Yao, S. (2016). Cognitive vulnerability to major depression: view from the intrinsic network and cross-network interactions. *Harvard review of psychiatry*, *24*(3), 188-201. https://doi.org/10.1097/HRP.0000000000000081

Wang, Y. P., & Gorenstein, C. (2013). Psychometric properties of the Beck Depression Inventory-II: a comprehensive review. *Brazilian Journal of Psychiatry*, *35*, 416-431. https://doi.org/10.1590/1516-4446-2012-1048

Waseem, R. (2017). *Cross-cultural equivalence of Beck Depression Inventory-II (BDI-II) for Pakistani Canadian immigrants and others* (Doctoral dissertation, University of British Columbia).

Weber, S., Bühler, J., Messmer, F., Bruckmaier, R., & Aybek, S. (2024). Cortisol in functional neurological disorders: State, trait and prognostic biomarkers. *Journal of Psychosomatic Research*, 111615. https://doi.org/10.1016/j.jpsychores.2024.111615

Weber, S., Bühler, J., Vanini, G., Loukas, S., Bruckmaier, R., & Aybek, S. (2023). Identification of biopsychological trait markers in functional neurological disorders. *Brain*, *146*(6), 2627-2641. https://doi.org/10.1093/brain/awac442

Weber, S., Heim, S., Richiardi, J., Van De Ville, D., Serranová, T., Jech, R., ... & Aybek, S. (2022). Multi-centre classification of functional neurological disorders based on resting-state functional connectivity. *NeuroImage: Clinical*, *35*, 103090. https://doi.org/10.1016/j.nicl.2022.103090

Wegrzyk, J., Kebets, V., Richiardi, J., Galli, S., Van de Ville, D., & Aybek, S. (2018). Identifying motor functional neurological disorder using resting-state functional connectivity. *NeuroImage: Clinical*, *17*, 163-168. https://doi.org/10.1016/j.nicl.2017.10.012

Wendell, S. (1996). *The rejected body: Feminist philosophical reflections on disability*. Routledge. https://doi.org/10.4324/9780203821069

Werner, N. S., Peres, I., Duschek, S., & Schandry, R. (2010). Implicit memory for emotional words is modulated by cardiac perception. *Biological psychology*, *85*(3), 370-376. https://doi.org/10.1016/j.biopsycho.2010.08.008

Whitlock, F. A. (1967). The aetiology of hysteria. *Acta Psychiatrica Scandinavica*, *43*(2), 144-162. https://doi.org/10.1111/j.1600-0447.1967.tb11023.x

Whoqol Group. (1998). Development of the World Health Organization WHOQOL-BREF quality of life assessment. *Psychological medicine*, *28*(3), 551-558. https://doi.org/10.1017/S0033291798006667

Wieder, L., & Terhune, D. B. (2019). Trauma and anxious attachment influence the relationship between suggestibility and dissociation: A moderated-moderation analysis. *Cognitive neuropsychiatry*, *24*(3), 191-207. https://doi.org/10.1080/13546805.2019.1606705

Wild, EJ; Tabrizi, SJ; (2007) The differential diagnosis of chorea. Practical Neurology , 7 (6) 360 - 373. 10.1136/pn.2007.134585. https://doi.org/10.1136/pn.2007.134585

Williams, B., Ospina, J. P., Jalilianhasanpour, R., Fricchione, G. L., & Perez, D. L. (2019). Fearful attachment linked to childhood abuse, alexithymia, and depression in motor functional neurological disorders. *The Journal of neuropsychiatry and clinical neurosciences*, *31*(1), 65-69. https://doi.org/10.1176/appi.neuropsych.18040095

Williams, I. A., Levita, L., & Reuber, M. (2018). Emotion dysregulation in patients with psychogenic nonepileptic seizures: a systematic review based on the extended process model. *Epilepsy & Behavior*, *86*, 37-48. https://doi.org/10.1016/j.yebeh.2018.06.049

Williams, I. A., Reuber, M., & Levita, L. (2020). Interoception and stress in patients with Functional Neurological Symptom Disorder. *Cognitive Neuropsychiatry*, 1-20. https://doi.org/10.1136/jnnp-2019-BNPA.24

Williams, I. A., Reuber, M., & Levita, L. (2021). Interoception and stress in patients with Functional Neurological Symptom Disorder. *Cognitive neuropsychiatry*, *26*(2), 75–94. https://doi.org/10.1080/13546805.2020.1865895

Williams, L. M. (2017). Defining biotypes for depression and anxiety based on large-scale circuit dysfunction: A theoretical review of the evidence and future directions for

clinical translation. *Depression and anxiety*, *34*(1), 9-24. https://doi.org/10.1002/da.22556

Williams, Z. J., & Gotham, K. O. (2021). Improving the measurement of alexithymia in autistic adults: A psychometric investigation of the 20-item Toronto Alexithymia Scale and generation of a general alexithymia factor score using item response theory. *Molecular autism*, *12*(1), 56. https://doi.org/10.1080/13546805.2020.1865895

Williams, Z. J., Everaert, J., & Gotham, K. O. (2021). Measuring Depression in Autistic Adults: Psychometric Validation of the Beck Depression Inventory-II. *Assessment*, *28*(3), 858–876. https://doi.org/10.1177/1073191120952889

Williamson, J. C., & Larner, A. J. (2018). Attended with and head-turning sign can be clinical markers of cognitive impairment in older adults. *International Psychogeriatrics*, *30*(10), 1569-1569. https://doi.org/10.1017/S1041610218000121

Windle, G., Bennett, K.M. & Noyes, J. A methodological review of resilience measurement scales. *Health Qual Life Outcomes* **9**, 8 (2011). https://doi.org/10.1186/1477-7525-9-8

Winterdahl, M., Miani, A., Vercoe, M. J., Ciovica, A., Uber-Zak, L., Rask, C. U., & Zak, P. J. (2017). Vulnerability to psychogenic non-epileptic seizures is linked to low neuropeptide Y levels. *Stress*, *20*(6), 589-597. https://doi.org/10.1080/10253890.2017.1378638

Wohleb, E. S., Franklin, T., Iwata, M., & Duman, R. S. (2016). Integrating neuroimmune systems in the neurobiology of depression. *Nature Reviews Neuroscience*, *17*(8), 497-511. https://doi.org/10.1038/nrn.2016.69

Wolf, R. C., Sambataro, F., Vasic, N., Schmid, M., Thomann, P. A., Bienentreu, S. D., & Wolf, N. D. (2011). Aberrant connectivity of resting-state networks in borderline personality disorder. *Journal of Psychiatry and Neuroscience*, *36*(6), 402-411. https://doi.org/10.1503/jpn.100150

Wong, M., Looney, E., Michaels, J., Palesh, O., & Koopman, C. (2006). A preliminary study of peritraumatic dissociation, social support, and coping in relation to posttraumatic stress symptoms for a parent's cancer. *Psycho-oncology*, *15*(12), 1093-1098. https://doi.org/10.1002/pon.1041

Woolf, S. H. (2008). The meaning of translational research and why it matters. *JAMA, 299*(2), 211–213. https://doi.org/10.1001/jama.2007.26

World Health Organisation. (1992). The ICD-10 classification of mental and behavioural disorders: Clinical descriptions and diagnostic guidelines.

World Health Organization. (2018). International statistical classification of diseases and related health problems (11th ed.). https://icd.who.int/en

World Health Organization. ICD-11: International Classification of Diseases 11th Revision . WHO, 2019.

Xue, Q., Wang, Z. Y., Xiong, X. C., Tian, C. Y., Wang, Y. P., & Xu, P. (2013). Altered brain connectivity in patients with psychogenic non-epileptic seizures: a scalp electroencephalography study. *Journal of international medical research*, *41*(5), 1682-1690. https://doi.org/10.1177/0300060513496170

Yim, Y. R., Lee, K. E., Park, D. J., Kim, S. H., Nah, S. S., Lee, J. H., ... & Lee, S. S. (2017). Identifying fibromyalgia subgroups using cluster analysis: Relationships with clinical variables. *European Journal of Pain*, *21*(2), 374-384. https://doi.org/10.1002/ejp.935

Yogarajah, M., Koreki, A., Agrawal, N., Cope, S., Eilon, T., Van Praag, C. G., Garfkinel, S., Critchley, H., Mula, M., & Edwards, M. (2019). 17 State and trait interoception is disrupted in functional seizures. https://doi.org/10.1136/jnnp-2019-BNPA.17

Yong, K., Chin, R. F., Shetty, J., Hogg, K., Burgess, K., Lindsay, M., ... & Pilley, E. (2023). Functional neurological disorder in children and young people: Incidence, clinical features, and prognosis. *Developmental Medicine & Child Neurology*, *65*(9), 1238-1246. https://doi.org/10.1111/dmcn.15538

Young, C. B., Chen, T., Nusslock, R., Keller, J., Schatzberg, A. F., & Menon, V. (2016). Anhedonia and general distress show dissociable ventromedial prefrontal cortex connectivity in major depressive disorder. *Translational psychiatry*, *6*(5), e810-e810. https://doi.org/10.1038/tp.2016.80

Young, E. A., Abelson, J., & Lightman, S. L. (2004). Cortisol pulsatility and its role in stress regulation and health. *Frontiers in neuroendocrinology*, *25*(2), 69-76. https://doi.org/10.1016/j.yfrne.2004.07.001

Yulmetyev, R. M., Demin, S. A., & Hänggi, P. (2006). Manifestation of chaos in real complex systems: Case of parkinson's disease. In *The logistic map and the route to chaos: From the beginnings to modern applications* (pp. 175-196). Berlin, Heidelberg: Springer Berlin Heidelberg. https://doi.org/10.1007/3-540-32023-7_11

Zamariola, G., Frost, N., Van Oost, A., Corneille, O., & Luminet, O. (2019). Relationship between interoception and emotion regulation: New evidence from mixed methods. *Journal of Affective Disorders*, *246*, 480-485. https://doi.org/10.1016/j.jad.2018.12.101

Zhang, D., Yuan, T., Huang, A., Li, X., Yang, L., Wang, C., Liu, M., Lei, Y., Sun, L., Li, J., Zhang, L., & Zhang, J. (2024). Validation of the Chinese version of the Oslo-3 Social Support Scale among nursing students: a study based on Classical Test Theory and Item Response Theory models. *BMC nursing*, *23*(1), 360. https://doi.org/10.1186/s12912-024-02033-5

Zhu, X., Wang, X., Xiao, J., Liao, J., Zhong, M., Wang, W., & Yao, S. (2012). Evidence of a dissociation pattern in resting-state default mode network connectivity in first-episode, treatment-naive major depression patients. *Biological psychiatry*, *71*(7), 611-617. https://doi.org/10.1016/j.biopsych.2011.10.035

Zito, G. A., Wiest, R., & Aybek, S. (2020). Neural correlates of sense of agency in motor control: A neuroimaging meta-analysis. *PLoS One*, *15*(6), e0234321. https://doi.org/10.1371/journal.pone.0234321

Zutt, R., Elting, J. W., Van der Hoeven, J. H., Lange, F., & Tijssen, M. A. J. (2017). Myoclonus subtypes in tertiary referral center. Cortical myoclonus and functional jerks are common. *Clinical Neurophysiology*, *128*(1), 253-259. https://doi:10.1016/j.clinph.2016.10.093